IUCLID

Data Set

Existing Chemical	:	ID: 147732-60-3
CAS No.	:	147732-60-3
Producer Related Part		
Company	:	The Dow Chemical Company
Creation date	:	13.08.2001
Substance Related Part		
Company	:	The Dow Chemical Company
Creation date	:	13.08.2001
Memo	:	
Printing date	:	15.12.2003
Revision date	:	
Date of last Update	:	15.08.2002
Number of Pages	:	55
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	???

1.0.1 OECD AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE

Name of Plant	:	Pilot Chemical
Street	:	606 Shepherd Drive
Town	:	45215 Lockland, Ohio
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	

21.01.2002

Name of Plant	:	Pilot Chemical
Street	:	3439 Yankee Road
Town	:	45042 Middletown, Ohio
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	

07.06.2002

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

Substance type	:	organic
Physical status	:	liquid
Purity	:	% w/w
Test substance	:	This product is normally sold as an aqueous solution. The solid is also a mixture of isomers conforming to the generic description.

13.08.2001

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

Benzene, 1,1'-oxybis-, sec-hexyl derivatives, sulfonated, sodium salts
14.08.2001

C6 Dowfax
13.08.2001

Dowfax C-6 Surfactant
13.08.2001

Dowfax C6 Surfactant

13.08.2001

Dowfax C6L Surfactant
13.08.2001

Dowfax Dry Hydrotrope Powder
13.08.2001

Dowfax XD 8292
13.08.2001

Dowfax* Dry Hydrotrope Powder (dry form of XD-8292)
08.01.2002

Sodium mono- and dihexyl diphenyl oxide disulfonate
14.08.2001

1.3 IMPURITIES

CAS-No : 7757-82-6
EINECS-No : 231-820-9
EINECS-Name : sodium sulphate
Contents : < 3 % w/w
14.08.2001

CAS-No : 7647-14-5
EINECS-No : 231-598-3
EINECS-Name : sodium chloride
Contents : < 3 % w/w
14.08.2001

1.4 ADDITIVES

Remark : The commercial product is normally an aqueous solution containing about 50% water.

14.08.2001

1.5 QUANTITY

Production during the last 12 months :
Import during the last 12 months :
Quantity produced : 100 - 500 tonnes in 1999
Remark : Amount shown is amount sold globally.
04.06.2002

1.6.1 LABELLING

Labelling : provisionally by manufacturer/importer
Symbols : XiN
Nota :
Specific limits :
R-Phrases : (36) Irritating to eyes
(51) Toxic to aquatic organisms

(53) May cause long-term adverse effects in the aquatic environment

S-Phrases : (61) Avoid release to the environment. Refer to special instructions/Safety data sets

14.08.2001

1.6.2 CLASSIFICATION

Classification : provisionally by manufacturer/importer
Class of danger : irritating
R-Phrases : (36) Irritating to eyes
(51) Toxic to aquatic organisms
(53) May cause long-term adverse effects in the aquatic environment

14.08.2001

1.7 USE PATTERN

Type : use
Category : Surface-active agents

29.10.2001

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

Memo : Occupational Exposure
Remark : Due to lack of data concerning the fraction of applied dermal dose which is absorbed, dermal 'doses' should be viewed as maxima.
The substance is mainly used (37%) in the manufacture of emulsion polymers with at least 28% going into the public domain as part of paint and coating formulations, household cleaners and industrial and institutional cleaners. In the mineral, oil and fuel indistry it is used as a viscosity adjustor, in the pulp, paper, and board indistry it is used as process regulator, and in the polymer indistry it is used as a hydrotrope and process regulator. In most applications the substance is used in diluted form: a stock solution containing up to 2.4% of the active ingredient is further diluted by a factor of approximately 20.

Inhalation and dermal exposure to the substance is possible during blending and application. Ocular exposure due to hand-eye contact cannot be excluded during these operations.

Exposures could occur at two stages during dilution: by diluting the substance from 45% to 2.4% and dilution of the stock solution by a factor of 20 and use of the stock solution.

07.06.2002

Memo : Preparation of a Stock Solution
Remark : The inhalation exposure in preparation of a stock solution by diluting the substance from 45 to 2.4% is assumed to be non-dispersive use in the presence of LEV. The EASE model estimates the exposure to be 0.5-3 ppm (10-60 mg/m3). The EASE model probably overestimates exposure because only ranges of vapor pressures are evaluated and the vapor

pressure of the substance is very close to the lower limit of the 'low' range. For compensation, the lower value of the range is used, 10 mg/m3. Assuming a pulmonary ventilation rate of 1.25 m3/hr and a job time of up to 1 hour, the daily dose is (1*1.25*10)12.5 mg/day.

Dermal exposure assuming non-dispersive use, direct handling and incidental contact is estimated to be 0-0.1 cm2/day. Assuming an exposed area of 420 cm2 (part of both hands), the daily dose is (0.1*420) = 42 mg/day.

07.06.2002

Memo : Dilution and Use of a Stock Dilution
Remark : Diluting a stock solution (2.4% for industrial cleaning is considered to be wide dispersive use with direct handling. Inhalation exposure is estimated to be negligible due to the low vapor pressure of the substance and the low percentage of the substance in the stock solution. Dermal exposure assuming wide dispersive use and direct handling with intermittent contact, is 1-5 mg/cm2/day. With an exposed area of 420 cm2 the daily dose is (5*0.024*420) = 50 mg/day.

The number of persons and frequency of use may differ greatly in the two scenarios. Batches of stock solution are made in a frequency of 2-20 batches per year (industry data), depending on the category of industry. A limited number of persons will be involved -- 10-20 (expert judgment). As an ingredient in industrial cleaning the frequency may be up to once a week involving 200-500 persons (both expert judgment).

07.06.2002

Memo : Consumer Exposure
Remark : This substance is used in cleaning and washing agents. The amin route of potential exposure by consumers is via skin contact. In view of the low log Kow (</= -3.5) the dermal availability is considered to be negligible. However, it should be noted that the substance is an eye irritant.

07.06.2002

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

Type : Handling
Remark : Provide general and/or local exhaust ventilation to control airborne levels below the exposure guidelines (for sodium sulfate and sodium chloride).

Atmospheric levels should be maintained below the exposure guidelines (for sodium sulfate and sodium chloride).
When respiratory protection is required for certain operations, use an approved air-purifying respirator.

No precautions other than clean body-covering clothing should be needed.

Use chemical goggles.

14.08.2001

Type : Fire
Remark : No fire or explosion hazards known. No flammable limits or flash point for the aqueous solution.

The organic portion may burn once the water is evaporated. In such case, use water for extinguishing media.

Wear positive-pressure, self-contained breathing apparatus.

14.08.2001

14.08.2001

Type : Storage
Remark : Stable at ambient temperatures.
Avoid unintended contact with acids.
Hazardous Decomposition Products: Sulfur dioxide
Hazardous polymerization will not occur.

14.08.2001

1.10.2 EMERGENCY MEASURES

Type : accidental spillage
Remark : Spills should be collected to prevent contamination of waterways.

Contain spill if possible. Absorb with material such as sawdust, kob grit and Zorb-all(R).

14.08.2001

Type : injury to persons (skin)
Remark : Wash off in flowing water or shower.

14.08.2001

Type : injury to persons (eye)
Remark : Irrigate with flowing water immediately and continuously for 15 minutes. Consult medical personnel.

14.08.2001

Type : injury to persons (oral)
Remark : If swallowed, seek medical attention. Do not induce vomiting unless directed to do so by medical personnel.

14.08.2001

Type : injury to persons (inhalation)
Remark : Remove to fresh air if effects occur. Consult a physician.

14.08.2001

Type : other
Remark : Note To Physician: No specific antidote. Supportive care. Treatment based on judgment of the physician in response to reactions of the patient.

14.08.2001

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

Memo : DO NOT DUMP INTO ANY SEWERS, ON THE GROUND OR INTO ANY BODY OF WATER. All disposal methods must be in compliance with all governmental laws and regulations.

14.08.2001

Memo : Waste characterizations and compliance with applicable laws are the responsibility solely of the waste generator.

14.08.2001

Memo : For unused and uncontaminated product, the preferred options include sending it to a licensed, permitted incinerator or other thermal destruction device.

14.08.2001

1.14.1 WATER POLLUTION

14.08.2001

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

Memo : Consumer Risk
Remark : Consumer exposure is expected. However, due to the low log Kow (< -3.5), absorption via skin is considered to be negligible.

07.06.2002

Memo : Man Exposed Indirectly via the Environment
Remark : A detailed risk assessment is not eprformed because:
-the PNEC is relatively high in view of the low toxicity (NOAEL = 50-250 mg/kg)
-the bioaccumulation potential is relatively low due to the low log Kow (</= -3.5).

As a consequence the margin of safety (MOS) for man exposed via the environment at the current tonnage level is expected to be >1000.

07.06.2002

Memo : Risk Characterization: Repeated Dose Toxicity
Remark : From the oral 28-day subacute toxicity study an NOAEL of 50-250 mg/kg/day is established (calculated using 250 as NOAEL because of questionably significant stomach irritation at 250). This level is used to estimate the risk for adverse systemic health effects. Extrapolation to humans (assuming 50% absorption from the gastrointestinal tract, 70 kg body weight, an extrapolation- and uncertainty factor of 1000) results in an internal Health-Based Occupational Reference Value for the worker (HBORV-intern) of 8.75 mg/day. Assuming 100% retention in the respiratory tract (worst case), a HBORV-inh of 8.75 mg/day is derived. Given the molecular weight and the octanol-water partition coefficient, it is expected that dermal absorption will not exceed 10%. For the risk estimation, 10% absorption is taken as a worst caseestimation, resulting in a HBORV-derm of 87.5 mg/day.

Scenario	Est. Exposure		Exceeding Factor	
	dermal (mg/day)	inhalation (mg/day)	derm	inh
Stock Prep	42	12.5	<1	1

Dil. of Stock	50	negl	<1	<1

Comparison of the HBORVs with exposure estimates leads to the conclusion that, for both occupational scenarios, the substance is of no concern for workers with respect to adverse systemic health effects after repeated dermal and/or inhalation exposures. It is noted that the risk for local effects after repeated dermal and inhalation exposure can only be estimated with results from toxicity studies performed with the respective exposure routes.

07.06.2002

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

Type : TSCA
Additional info :
14.08.2001

Type : EINECS
Additional info :
14.08.2001

Type : TSCA
Additional info :
14.08.2001

Type : PICCS
Additional info :
14.08.2001

Type : DSL
Additional info :
14.08.2001

2.1 MELTING POINT

Sublimation	:	
Method	:	other: EEC 92/69 EEC, Part A, L383, Dec. 1992
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	After a preliminary test to determine the melting range, the main study was performed with 2.05 mg of the substance in a sample container that was covered with a lid. This sample was heated with a rate of 10C/min in 3 runs: first from 35 to 200C, then from 150 to 250C and finally from 200 to 300C. Both the preliminary and main studies were performed under a flow of air (about 100 ml/min). After each experiment, the mass of the sample was measured and the sample was inspected visually.
Result	:	Up to about 150C part of Dowfax* dry hydrotrope powder (about 10%) evaporated. Between 215 and 232C a transition of the test substance (or part of it) from the glassy state to the undercooled liquid is observed. Between 265 and 280C a small exothermic effect is observed which may be caused by reaction or decomposition of the test substance or by crystallisation of (part of) the test substance. Reaction or decomposition of the test substance was certainly observed above 330C.
Test substance	:	The test substance was the dry hydrotrope powder of the C6 alkyl Dowfax XD-8292, CAS 147732-60-3, Lot 941205-134, min. 92% a.i.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

06.12.2001 (1)

Value	:	= 270 ° C
Sublimation	:	
Method	:	other:
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Melting Point, Boiling Point and Vapor Pressure estimated using Estimation Programs Interface (EPIWIN, Version 2, February 1997) available from Syracuse Research Corporation (Syracuse, NY). Estimations of properties for representative isomers are based on quantitative structure-activity relationships.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

11.03.2002 (2)

2.2 BOILING POINT

Value	:	= 610 ° C at
Decomposition	:	
Method	:	other:
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Melting Point, Boiling Point and Vapor Pressure estimated using Estimation Programs Interface (EPIWIN, Version 2, February 1997) available from Syracuse Research Corporation (Syracuse, NY). Estimations of properties for representative isomers are based on quantitative structure-activity relationships.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

29.10.2001 (3)

2.3 DENSITY

Type	:	density
Value	:	= 1.36 g/cm3 at 20° C
Method	:	Directive 84/449/EEC, A.3 "Relative Density"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	The test substance was dried for 4 days at room temperature in the dark in a desiccator, using silicagel as the agent. The test cell was pressurized to a pressure of slightly less than 20 psi (1.406 kg/cm3) and the pressure was read. Subsequently, an extra volume (V sub a) was added to the pressure system, resulting in a lower pressure, whichwas read after equilibration of the system. During the performance of the test, the temperature was measured. The volume of the calibration cell was determined, based on upper and lower pressure readings. The volume calibrations were based on a chrome plated calibration cylinder with known volume. The sample cell volume was determined from pressure differential, as well. The sample cell was weighed, filled with the test substance and placed in the stereopycnometer. Then, the test was performed as outlined above, resulting in pressure readings p sub 7 and p sub 8 (upper and lower, resp.). Then the sample cell containing the test substance was reweighed to determine the mass of the tested material. Density was = amount of test substance (g) / V sub p.
Result	:	The density of Dowfax* Dry Hydrotrope Powder was determined using the gas comparison method. It was found to be 1.36 g/cm3 using this gas comparison pycnometer.
Test substance	:	The test substance was the dry hydrotrope powder of the C6 alkyl Dowfax XD-8292, CAS 147732-60-3, Lot 941205-134, min. 92% a.i.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

11.03.2002 (4)

2.3.1 GRANULOMETRY

Type of Distribution	:	other: visual, sieved and by laser diffraction
Precentile	:	
Method	:	other
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	Visual: This looked at the dry substance and in suspension in cyclohexane. (it dissolved in water and ethanol but not in cyclohexane after 2 hrs) The instrument was a microscope with 200 and 300x power. Sieve: 25.0 grams of the test substance was sieved through a 250 microm analytical sieve and then a 63 microm anlayutical sieve, using a Retsch mechanical sieving apparatus. The sieving was continued until < 0.1 g/min. passed the sieves. Laser Diffraction: An amount of the test substance was added to the

cyclohexane in the measuring cell until an obscuration ('turbidity') of 0.1 - 0.3 was reached. The particle size distribution was measured (using a 100 mm lense) with 20 seconds of sonication.

The determination was based on the OECD 110 Guideline.

Result : Sieve: < 63 microns: 21.5% (m/m)
63-250 microns: 74.9%
>250 microns: 3.6%

Laser Diffraction:
<2 microns: 0.4% (m/m)
2-5 microns: 2.4%
5-10 microns: 3.6%
10-20 microns: 12.1
20-50 microns: 49.3%
50-63 microns: 16.8%
>63 microns: 15.4%

Total 100%

Combined Results:

	MALVERN	Total
<2 microns: 0.4% (m/m) (x21.5/100)		: 0.1%
2-5 microns: 2.4%	"	: 0.5%
5-10 microns: 3.6%	"	: 0.8%
10-20 microns: 12.1%	"	: 2.6%
20-50 microns: 49.3%	"	: 10.6%
50-63 microns: 16.8%	"	: 3.6%
>63 microns: 15.4%	"	= 3.3%
Sieve 63-250 microns:		=74.9% 78.2%
>250 microns:		3.6%

100%

Test substance : The test substance was the dry hydrotrope powder of the C6 alkyl Dowfax XD-8292, CAS 147732-60-3, Lot 941205-134, min. 92% a.i. In this case, the report called the substance, "Dowfax* C6L"; it was a light tan powder.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

11.03.2002 (5)

2.4 VAPOUR PRESSURE

Value : = .02 hPa at 20° C

Decomposition :

Method OECD Guide-line 104 "Vapour Pressure Curve"

Year : 1999

GLP : yes

Test substance : other TS

Method : The 'Static Technique' was used. Static vapour pressure measurements were made with a capacitance manometer fitted with a 133 Pa capacitive sensor. The reference pressure at the right-hand side of the diaphragm of the pressure sensor was kept below 10-4 Pa. The temperature of the sample was measured with a platinum resistance thermometer.

The sample vessel was cleaned, dried and filled with approx. 0.4 g of the test sample. After attaching the vessel to the measuring set-up, it was evacuated during about 15 minutes. The measurements were started at 38.66C. After measurement 23, the temperature of the thermostatic bath in which the sample vessel is immersed was lowered to 29.80C and finally after measurement 44 to 23.66C. A total of 56 measurements was

performed.

Because the measured vapor pressures were > 0.1 Pa, no correction according to Bennett and Tompkins (Trans Faraday Soc., 1957, 53, 185) for thermal transpiration was made. The test substance was considered to show ideal behavior. Thus the vapor pressure curve was derived according to Clarke and Glew (Trans Faraday Soc., 1966, 62, 539). The vapor pressure at 20C was calculated from the vapor pressure curve.

Remark : The vapor pressure determined in this test is higher than that predicted by QSAR and higher than experience has indicated.

Result : The static technique was used for the determination of the vapor pressure at 20C. At the beginning of the test, the vapor pressure of the test substance increased slightly every next measurement. After measurement 5, this decrease became negligible and the vapor pressure was stable. Only data from the stationary phase were used for the final result.

Measurement	Temp (C) in (p)	Mean V.P. (+/- 2 sigma n-1) Pa	
6-23	38.66	1.87 +/-0.01	6.48 +/- 0.07
24-44	29.80	1.37 +/-0.01	3.95 +/-0.03
45-56	23.66	1.014+/-0.001	2.76 +/- 0.01

Fitting these data according to Clark & Glew gives a value of 2.209 Pa with 0.007 Pa for 2 sigma n-1.
The value in mmHg is 1.66 x10-2.

Test substance : The test substance was the dry hydrotrope powder of the C6 alkyl Dowfax XD-8292, CAS 147732-60-3, Lot 941205-134, min. 92% a.i.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

17.06.2002 (6)

Value : = 0 hPa at 25° C

Decomposition :

Method other (calculated)

Year : 2001

GLP : no

Test substance : as prescribed by 1.1 - 1.4

Method : Melting Point, Boiling Point and Vapor Pressure estimated using Estimation Programs Interface (EPIWIN, Version 2, February 1997) available from Syracuse Research Corporation (Syracuse, NY). Estimations of properties for representative isomers are based on quantitative structure-activity relationships.

Reliability : (2) valid with restrictions

Flag : Material Safety Dataset

17.06.2002 (3)

2.5 PARTITION COEFFICIENT

Log pow : <= -3.5 at ° C

Method other (calculated): Rekker

Year : 1998

GLP : yes

Test substance : other TS

Method : Dowfax* Dry Hydrotrope Powder is a mixture of four, sulfonate groups containing salts. Because it is not possible to bring the salt molecules in a non-ionised form by pH adjustment, both the flask-shaking method and the HPLC method are not applicable for the determination of the partition coefficient (n-octanol/water). Since the structures of the sulfonate groups containing salts 'are not precisely known', the Rekker calculation method could not be used either. Thus, the partition coefficient (n-octanol/water)

		was calculated from the water solubility and the n-octanol solubility of Dowfax* Dry Hydrotrope Powder. The solutions and the test material were protected from light as much as possible.
Result	:	The partition coefficient (Pow) of Dowfax* Dry Hydrotrope Powder was determined to be </= x 10 -4 (log Pow </= -3.5) as a quotient of the n-octanol solubility and water solubility.
Test substance	:	The test substance was the dry hydrotrope powder of the C6 alkyl Dowfax XD-8292, CAS 147732-60-3, Lot 941205-134, min. 92% a.i.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

11.03.2002 (7)

Log pow	:	= .6 at 25° C
Method		other (calculated)
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Partition coefficient in environmental pH range of 5 to 9 estimated using ACD/Log D program (Version 4.56, April 2000) available from ACD Labs (Toronto Canada). Estimations of Log P for representative isomers based on quantitative structure-activity relationships which account for dissociation as a function of pH.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

29.10.2001 (3)

2.6.1 WATER SOLUBILITY

Method	:	OECD Guide-line 105 "Water Solubility"
Year	:	1999
GLP	:	yes
Test substance	:	other TS
Method	:	In a preliminary test, 1000 microl double distilled water was added to 1.10 g of the test substance. The tube was vortexed for 1 minute and thereafter placed on a magnetic stirring device. The content of the tube was stirred overnight in a climate room of which the temperature was measured continuously using a thermohygrographic device. The resultant phase was observed visually.
Result	:	After 17 hours in the preliminary test, no undissolved test substance was observed. Thus, no main study was performed. Dowfax* Dry Hydrotrope Powder was determined to be miscible with water in at least a 1:1 (w/v) ratio at 19.5 C.
Test substance	:	The test substance was the dry hydrotrope powder of the C6 alkyl Dowfax XD-8292, CAS 147732-60-3, Lot 941205-134, min. 92% a.i.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

11.03.2002 (8)

Value	:	> 100000 mg/l at 25 ° C
Qualitative	:	of very high solubility
Pka	:	at 25 ° C
PH	:	ca. 5 - 9 at and ° C
Method	:	other:
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Water solubility in environmental pH range of 5 to 9 estimated based on product formulation information. Formulations contain 10 to 50% of surfactant in water. Therefore solubility >100,000 mg/L.
Reliability	:	(2) valid with restrictions

Flag : Material Safety Dataset
29.10.2001 (3)

2.6.2 SURFACE TENSION

Test type : Ring method
Value : = 34.2 mN/m at 20 ° C
Concentration : 1019 mg/l
Method : Directive 84/449/EEC, A.5
Year : 1998
GLP : yes
Test substance : other TS
Method : Glassware was washed with chromo-sulfuric acid. The measurement vessel was washed with hot chromo-sulfuric acid and then with syrupy phosphoric acid. Then glassware was rinsed in tap-water and in double-distilled water. The measuring ring was similarly washed and then heated above a flame.
The tensiometer was calibated.

The cleaned and rinsed measurement vessel was filled with the test solution. The measurement vessel was placed in a thermostated waterbath (20C) on the mobile sample table. The table was raised until the ring was immersed below the surface of th solution. Subsequently, the table was lowered until the ring was attached to the liquid surface. After some additional lowering of the table, the ring exerts a torque on the force measuring system. This torque was compensated for manually (via machine knob). Lowering of the table and subsequent compensation of the resulting torque were continued in small increments until the lamina broke, i.e., the upward force on the ring completely overcame the surface tension force and the ring was torn away from the surface. The surface tension was then recorded. After completing the measurement the ring was immersed below the surface again and the measurements were repeated until aconstant surface tension value was reached. The time passed since the solution was transferred to the measurement vessel was recorded for each determination.
Result : The surface tension of a solution of Dowfax* Dry Hydrotrope Powder in water at a concentration of 1.019 g/l is 34.2 mN/m. Based on the criteria as outlined in the guideline, it is concluded that Dowfax* Dry Hydrotrope Powder should be regarded as a surface active material.

The measured value from the apparatus required a correction (Harkins-Jordan Correction) determined from a published table. According to the criteria as outlined in the EEC Directive, substances showing a surface tension lower than 60 mN/m under the conditions of this method, should be regarded as being surface active materials.
Test substance : The test substance was the dry hydrotrope powder of the C6 alkyl Dowfax XD-8292, CAS 147732-60-3, Lot 941205-134, min. 92% a.i. An aqueous solution of this powder was prepared by dissolving 101.9 mg test substance in 10 ml milli-Q water.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
24.04.2002 (9)

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

Value	:	> 400 ° C at
Method	:	Directive 84/449/EEC, A.16 "Auto-flammability of solids"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	The test oven and recorder were calibrated periodically using a calibrated digital thermometer. During the calibration procedure, the temp. rise, temp reading of the recorder and the temp. of the oven were evaluated. The 'cube' was completely filled witht the test substance. The sample was suspended in the center of the oven at room temperature. One thermocouple was placed at the center of the cube and the other between the cube and the oven wall to record the oven temp. The temperatures of the oven and sample were continuously recorded while the temperature of the oven was increased to 400 C at a rate of 0.5 C/min. At the end of the test, the consistency of the test substance was determined. If an exoothermic reaction occurs, the sample thermocouple shows a sharp temperature rise above the oven temp. The temperature of the oven at which the sample reaches 400C by self-heating is appointed as the self-ignition temperature of the test substance.
Result	:	No self-ignition occurred. The test substance changed into a grey/brown residue. Thus, according to the directive criteria, Dowfax* Dry Hydrotrope Powder is not self-ignitable.
Test substance	:	The test substance was the dry hydrotrope powder of the C6 alkyl Dowfax XD-8292, CAS 147732-60-3, Lot 941205-134, min. 92% a.i.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

11.03.2002 (10)

2.9 FLAMMABILITY

Result	:	other: not 'highly flammable'
Method	:	Directive 84/449/EEC, A.10 "Flammability (solids)"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	Dowfax* Dry Hydrotrope Powder was formed into a wedge-shaped pile with a length of 25 cm, a width of 2 cm and 1 cm in height. An attempt was made to ignite the test substance with a flame of a gas-burner. This was a preliminary test and after noting the results, no main study was necessary.
Result	:	Dowfax* Dry Hydrotrope Powder could be ignited with a flame, but no propagation throughout the test substance pile was observed. The test substance burned with an orange flame, colored black and emitted black smoke in contact with the ignition source. After removal of the ignition source, the test substance burned for another 20 seconds. Thus this dry form of the product is not 'highly flammable' according to this test.
Test substance	:	The test substance was the dry hydrotrope powder of the C6 alkyl Dowfax XD-8292, CAS 147732-60-3, Lot 941205-134, min. 92% a.i.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

24.04.2002 (11)

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= 13 hour(s)
Degradation	:	% after
Quantum yield	:	
Deg. product	:	
Method	:	other (calculated): AOP v1.91
Year	:	2006
GLP	:	
Test substance	:	

Result : SMILES: c1(Oc2c(C(C)CCCC)cc(S(O)(O)O)cc2)ccc(S(O)(O)O)cc1
Mol Formula: C18 H26 O7 S2
Mol Wt: 418.52

SUMMARY (AOP v1.91): HYDROXYL RADICALS
Hydrogen Abstraction = 6.6957 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 0.8400 E-12 cm3/molecule-sec
Addition to aromatic rings = 2.3179 E-12 cm3/molecule-sec

Overall OH Rate Constant = 9.8535 E-12 cm3/molecule-sec
Half life = 1.085 Days (12-hour day, 1.5E6 OH/cm3)
Half life = 13.026 Hours
2f: Accepted calculation method

25.07.2006

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	at degree C
t1/2 pH9	:	at degree C
Degradation	:	< 6 % after 5 day at pH and degree C
Deg. Product	:	
Method	:	OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	An accurately weighed amount of the test material (range 101.9-105.5 mg) was added to 50.0 ml buffer solution (pH 4.0, 7.0 and 9.0). The filter-sterilized solutions were treated for 5 minutes with nitrogen gas to exclude oxygen. The incubation took place at 50 C in the dark. The concentration of the test substance was determined by HPLC after 0, 2.4 hours and 5 days (quantification was based ont he major component of Dowfax). pH values were checked at the same time points.
Result	:	Dowfax* Dry Hydrotrope Powder showed no significant decrease in concentration after incubation at 50 C at pH 4.0, 7.0 or 9.0 for up to 5 days. At pH 4.0 still 94% of the original concentration could be found after 5 days, whereas for pH 7.0 and 9.0 the 5-day figures were 98% and 101%, respectively. Correspondingly, the material can be termed to be hydrolytically stable.
Test substance	:	The test substance was Dowfax* Dry Hydrotrope Powder.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
24.04.2002 (12)

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level I
Media :
Air : .1 % (Fugacity Model Level I)
Water : 99.6 % (Fugacity Model Level I)
Soil : .4 % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :

Attached document : Input Parameters for Level I Model:

Property	Value	Source
Data Temperature (°C)	25	
Chemical Type	1	Type 1 indicates chemical can partition into all environmental compartments
Molecular Mass (g/mol)	459	Calculated from molecular structure
Water Solubility (g/m^3)	100,000	Estimated value based on formulation composition [2]
Vapor Pressure @ 25°C (Pa)	1×10^{-12}	Estimated value [3]
Melting Point (°C)	270	Estimated value [3]
Log K_{ow} Octanol-Water Partition Coefficient	0.6	Estimated value [4]
Amount of Chemical input (kg)	100,000	Level I Default Value [1]

RESULTS

Fugacity Level I: Distribution among air, water, soil, and sediments

Emission Scenario	Percentage and amount distributed to			
	Air	Water	Soil	Sediment
100,000 kg total emissions	<0.1 % <1 kg	99.6 % 99641 kg	0.4 % 351 kg	<0.1 % 8 kg

1. Mackay, D. (2001). Multimedia Environmental Models: The Fugacity Approach. Lewis Publishers, CRC Press, Boca Raton, Florida. Models available at: http://www.trentu.ca/cemc/models.html
2. IUCLID Data Set for DOWFAX C6L Surfactant. December 17, 2002.
3. U.S. EPA. 2000. EPIWIN software, version 3.11. United States Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D. C. Available at: http://www.epa.gov/oppt/exposure/docs/episuitedl.htm
4. Advanced Chemistry Development, Inc., Toronto, Canada. 2000. ACD/Log D. Version 4.56.
5. European Commission. (1996). Technical Guidance Documents in support of the commission directive 93/67/EEC on risk assessment for new notified substances and commission regulation. European Commission, Brussels, Belgium.

Conclusion : Dowfax C6L surfactant has little potential to volatilize from aqueous solution, based on the very low estimated Henry's Law constant (5 x 10(-15) Pa m(3)/mol). The compound has a low potential to bioaccumulate in

aquatic organisms based on the estimated log Kow value (0.6).

Distribution of surface active agents (i.e. surfactants) is governed by interfacial distributions and not by equilibrium partitioning. Thus, the outcome of the Level 1 fugacity models for Dowfax C6L surfactant are speculative at best. Also, note that DOWFAX C6L surfactant will be ionized in solution due to the low pKa of the sulfonate groups (estimated pKa <2). Therefore, partitioning from water to air (i.e. volatilization) or from water to organic phases (i.e. octanol/water partition coefficient) may be significantly less than that predicted for the neutral (uncharged) molecule.

Reliability : (2) valid with restrictions
2f: Accepted calculation method

12.06.2006

Type : fugacity model level III
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :

Attached document : Input Parameters for Level III Model:

Property	Value	Source
Data Temperature (°C)	25	
Chemical Type	1	Type 1 indicates chemical can partition into all environmental compartments
Molecular Mass (g/mol)	459	Calculated from molecular structure
Water Solubility (g/m^3)	100,000	Estimated value based on formulation composition [2]
Vapor Pressure @ 25°C (Pa)	1×10^{-12}	Estimated value [3]
Melting Point (°C)	270	Estimated value [3]
Estimated Henry's Law Constant (H) ($Pa\ m^3/mol$)	4.6×10^{-15}	Calculated by Level I Fugacity Model [1]
Log K_{ow} Octanol-Water Partition Coefficient	0.6	Estimated value [4]
Amount of Chemical input (kg/hr)	1,000 per compartment	Level III Default Values [1]
Reaction Half-lives (hr) Input to Level III Model		
Air (vapor phase)	*32	Estimated value [3]
Water (no susp. solids)	3600	Estimated value [5]
Soil	7200	Estimated value [5]
Sediment	7200	Estimated value [5]
Suspended Sediment	$**1.0 \times 10^{11}$	
Fish	$**1.0 \times 10^{11}$	
Aerosol	$**1.0 \times 10^{11}$	

**Default value used in Level III model when reaction is expected to be negligible in this compartment

Fugacity Level III: Distribution among air, water, soil, and sediments

Emission Scenario	Percentage and amount distributed to: Air	Water	Soil	Sediment	Residence Time (days) [without advection in brackets]
1,000 kg/hr to Air	<0.1 % <1 kg	56.4 % 7.89×10^5 kg	43.6 % 6.10×10^5 kg	<0.1 % 326 kg	58 [277]
1,000 kg/hr to Water	**<0.1 % <1 kg**	**100.0 % 8.39×10^5 kg**	**<0.1 % <1 kg**	**<0.1 % 346 kg**	**35 [216]**
1,000 kg/hr to Soil	<0.1 % <1 kg	55.3 % 7.87×10^5 kg	44.7 % 6.37×10^5 kg	<0.1 % 325 kg	59 [279]
1,000 kg/hr simultaneously to Air, Water, and Soil	<0.1 % <1 kg	65.9 % 2.42×10^6 kg	34.0 % 1.25×10^6 kg	<0.1 % 998 kg	51 [261]

Highlighted scenario indicates most likely emission distribution, based on use patterns

1. Mackay, D. (2001). Multimedia Environmental Models: The Fugacity Approach. Lewis Publishers, CRC Press, Boca Raton, Florida. Models available at:

http://www.trentu.ca/cemc/models.html
2. IUCLID Data Set for DOWFAX C6L Surfactant. December 17, 2002.
3. U.S. EPA. 2000. EPIWIN software, version 3.11. United States Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D. C. Available at: http://www.epa.gov/oppt/exposure/docs/episuitedl.htm
4. Advanced Chemistry Development, Inc., Toronto, Canada. 2000. ACD/Log D. Version 4.56.
5. European Commission. (1996). Technical Guidance Documents in support of the commission directive 93/67/EEC on risk assessment for new notified substances and commission regulation. European Commission, Brussels, Belgium.

Conclusion : DOWFAX C6L Surfactant has little potential to volatilize from aqueous solution, based on the very low estimated Henry's Law constant (5 x 10-15 Pa m3/mol). The compound has a low potential to bioaccumulate in aquatic organisms based on the estimated log Kow value (0.6). Major applications for the alkyl diphenyl oxide disulfonate surfactants include emulsion polymerization and institutional and industrial cleaning. Based on the physical and chemical properties and known uses of DOWFAX C6L Surfactant, the compound will be released primarily into water. Assuming release into water only, the Level III fugacity model predicts that the compound will remain in the water compartment with a residence time of approximately 35 days. Advection is the major process that affects the predicted residence time for the compound.

Distribution of surface active agents (i.e. surfactants) is governed by interfacial distributions and not by equilibrium partitioning. Thus, the output of the Level III fugacity models for DOWFAX C6L Surfactant are speculative, at best. Also, note that DOWFAX C6L Surfactant will be ionized in solution due to the low pKa of the sulfonate groups (estimated pKa <2 [4]). Therefore, partitioning from water to air (i.e. volatilization) or from water to organic phases (i.e. octanol/water partition coefficient) may be significantly less than that predicted for the neutral (uncharged) molecule.

Reliability : (2) valid with restrictions
2f: Accepted calculation method

12.06.2006

Type : other: adsorption/desorption
Media :
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : other: OECD 106
Year : 1998
Method : For the investigation of the adsorption behavior, three different soils were used: 1) Cranfield 164 soil (3.4% organic matter; pH 7.2; 13.2% clay, 73.8% silt and 13.0% sand). 2) Midwest 2 soil (1.0% organic matter; pH 5.9; 6% clay, 8% silt and 86% sand). 3) Cranfield 115 soil (2.8 % organic matter; pH 8.1, 32.2% clay, 23.1% silt and 44.9% sand). The soils were first equilibrated with water. To approx. 5 g of each equilibrated soil approx. 10 ml of an aqueous solution of the test material (4.5 mg/l in 0.01 M CaCl2) was added (3 parallel samples per soil). Incubation took place at 20C on a shaker over a period of 16 hours. Subsequently, the vials were centrifuged (5 min, 170 x g). The supernatants were removed, weighed and an aliquot centrifuged for 5 minutes at 3500 xg. The amount of residual test material still present in the supernatant after incubation (adsorption) was analyzed with HPLC. To follow the desorption of the test material 10 ml of 0.01 M CaCl2 solution was added to the treated soil samples containing the Cranfield 164 soil. For the other soils the desorption step was omitted due to limited sorption in the first place. The vials were again

shaken for 16 hours at 20C followed by centrifugation (5 min., 170 x g) and HPLC analysis fo the 3500 x g supernatants.

Result : The Koc values were:

Cranfield 164 12.3 ccm/g
Midwest 2 5.3 ccm/g
Cranfield 115 0 ccm/g

Because of the low amount of the test material adsorbed to Cranfield 164 soil (0-8%) desorption could not be determined. These results indicate that Dowfax Dry Hydrotrope Powder can be considered to be highly mobile in soil.

Test substance : The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
24.04.2002 (13)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 20.7mg/l related to Test substance
12mg/l related to COD (Chemical Oxygen Demand)
Contact time : 28 day
Degradation : ca. 0 % after 28 day
Result : under test conditions no biodegradation observed
Control substance : Acetic acid, sodium salt
Kinetic : %
%
Deg. Product :
Method : Directive 84/449/EEC, C.4 "Biotic degradation - modified AFNOR test NF T90/302"
Year : 1998
GLP : yes
Test substance : other TS
Method : The study was conducted with glass culture vessels that contained 2 liters of mineral medium. The vessels were maintained in the dark at 21C for 28 days and aerated with CO2-free air. An aliquot of the supernatant of washed, settled municipal sludge was added as inoculum. The test substance was incubated in the nutrient medium at a concentration of 20.7 mg/L (corresponding to 12 mg/l Total Organic Carbon (TOC); two parallel samples). Concurrent controls consisted of nutrient medium plus inoculum alone (blank), nutrient medium with 40.15 mg/L sodim acetate (12 mg/l TOC; positive control) as well as a toxicity control with test and reference substance together (same concentration as in the individual samples discribed above). Degradation was measured by total inorganic carbon analysis of evolved CO2 absorbed with 0.0125 M Ba(OH)2 in gas scrubbing bottles in multiple samples from day 0 through day 28. The percentage degradation was calculated from the throretical CO2 content (ThCO2) of the test material (2.14 mg/l).
Result : Dowfax* Dry Hydrotrope Powder showed no significant biodegradation after 28 days. The sodium acetate control attained 60% degradation after 14 days which confirmed the suitability of the inoculum and test conditions.

		The toxicity control showed more than 25% biodegradation within 14 days (absence of significant inhibitory effects by the test material). Based on these results Dowfax* Dry Hydrotrope Powder cannot be considered as readily biodegradable under the strict terms and conditions of the CO2 Evolution Test.
Test condition	:	The temperature of a vessel in the same room with the test vessel varied between 20 and 22C. The pH of all vessels were 7.6 and on day 28, they were 7.7 for the blank controls and the Dowfax vessels and 8.0 for the toxicity and positive controls. The positive control was degraded by 60% of day 14; the total CO2 released in the blank reached a total of 20 mg CO2/2 liters; and the difference of duplicate values for %-degradaiton of Dowfax was always <20. Thus the criteria for acceptability of the test were met.
Test substance	:	The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

15.08.2002 (14)

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Concentration	:	20mg/l related to Test substance related to
Contact time	:	
Degradation	:	ca. 73 % after 21 day
Result	:	other: did meet the pass level of 80% in the CAS test
Control substance	:	other: potassium hydrogen phthalate
Kinetic	:	**%** **%**
Deg. Product	:	
Method	:	OECD Guide-line 303 A "Simulation Test - Aerobic Sewage Treatment: Coupled Unit Test"
Year	:	1999
GLP	:	yes
Test substance	:	other TS
Method	:	Two small OECD Confirmatory Test units containing 360 ml medium in the aeration vessel were run in parallel without being coupled (no sludge exchange). The test material was dissolved in settled domestic sewage which was collected from a municipal waste water treatment plant at weekly intervals. Settled sewage and test material at a concentration of 20.0 mg/l were continuously fed to the aeration vessel of the first unit. A second unit where only settled sewage was continuously added served as a control. Both units contained activated sludge at a concentration of approx. 1.5 g/l (dry weight) during the relevant test period. Incubation took place at 21-23 deg.C in diffuse light. The hydraulic residence time (HRT) was kept at 6 hr whereas the sludge retention time (SRT) was 10 days. Effluents of both units were collected and aliquots used for determination of Methylene Blue Active Substance (MBAS). Primary biodegradation was calculated based on the percentage MBAS removal by comparing influent and effluent MBAS concentrations corrected by the effluent MBAS concentfration of the control unit.
Result	:	Upon addition of Dowfax* Dry Hydrotrope Powder a significant MBAS removal between 70 and 80% was observed. The percentage removal did not further increase during the following test period. A time window of three weeks was chosen to calculate the mean percentage of removal. The primary biodegradation based on MBAS removal measured during the specified 21 days reached a mean value of 73% (95% c.l.: +/- 4%). The test material did therefore, not pass the 80% level for primary biodegradation as required by the EU Detergent Directive (Council Directive 82/243/EEC).
Test condition	:	The test was performed in diffuse light. The incubation temperature of both CAS units ranged from 19.0 to 21.7C. The pH of the effluent of the CAS

units varied from 7.2 to 7.6. The oxygen concentrations measured were >4.7 mg/l.
The test met the performance criteria for validity.

Test substance : The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
15.08.2002 (15)

Type : aerobic
Inoculum :
Contact time :
Degradation : = 63.3 % after 19 day
Result :
Control substance : other: Marlon A
Kinetic : **%**
%
Deg. Product :
Method : other: 82/243/44C
Year : 1986
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Reliability : (2) valid with restrictions
Flag : Material Safety Dataset
20.08.2001 (16)

Type : aerobic
Inoculum :
Concentration : 2500mg/l related to
related to
Contact time : 7 day
Degradation : = 79.2 % after 7 day
Result : other
Control substance : other
Kinetic : **%**
%
Deg. Product :
Method :
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : Activated sludge from the E. Lansing, MI, municipal wastewater treatment plant was used. A positive control linear alkylbenzene sulfonate (LAS) was used. Aliquots of mixed liquor (1.5L) were dispensed into each of 10 SCAS cylinders (2/test substance) at a nominal TSS concentration of 2500 mg/L. An airflow rate of 500 cc/min was maintained in each cylinder.

Beginning the following morning and continuing throughout the study, the SCAS cylinders were operated on a 24-hour fill and drain cycle. Following 23 hours of aeration, the air flow to the SCAS cylinders was stopped and the activated sludge solids allowed to settle at least 30 min. One liter of clarified supernatant liquid was drained from each cylinder, replaced with one liter of synthetic sewage feed, and the aeration resumed. The synthetic sewage feed was prepared by diluting 10 ml of a synthetic sewage stock solution to one liter with tap water.

Aqueous solutions of the surfactants were prepared at nominal concentrations of 1.0 mg/ml and added to the appropriate synthetic sewage feed solutions as described.

Test Duration:
5 day surfactant build-up in feed
3 day equilibrium at 20 mg/l

7 days of operation with 20 mg/l surfactant in feed

Remark : Did not meet the criteria for biodegradability (90% reduction in methylene blue active substance following 23 hours of aeration).

Result : The 7 days % biodegradation was 79.0 for one cylinder and 79.4 for the other--which averages to 79.2 for both together.

Test substance : XDS 8292.00 -- A linear 6 carbon alkylated sulfonated diphenyl oxide; 45% active ingredient in water

Flag : Critical study for SIDS endpoint

24.04.2002 (17)

3.6 BOD5, COD OR BOD5/COD RATIO

COD

Method : other

Year : 1987

GLP : yes

COD : mg/g substance

Method : COD was determined using an acidic dichromate digestion procedure (Hach method). This procedure uses a high temperature acidic dichromate digestion of an aqueous solution of the test material followed by a spectrophotometric determination of unreacted dichromate. The latter value allows calculation of the COD of the test material. COD was determined by comparison to a standard LAS (linear alkylbenzene sulfonate) calibration curve.

Result : COD was reported as 1.91 parts of oxygen/part of product (on a 100% active basis)

24.04.2002 (17)

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	yes
LC50	:	= 6.8 (calculated)
Method	:	other: C.1 and OECD 203
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	Subsequent to a range-finding study, groups of 7 fish were exposed to aqueous solutions of the test material at nominal concentrations of 0.22, 0.46, 1.0, 2.2, 4.6 and 10.0 mg/l; an additional group of 7 fish was included as untreated control. The fish were exposed for 96 hours in 4 L glass aquaria that contained 3 L of test media; the exposure method was static. The fish were observed for mortality and other effects at 2, 24, 48, 72 and 96 hours of exposure. The temperature, pH and oxygen concentration of the test solutions were monitored throughout the study. Samples were taken for analysis at 0 and 96 hours from the vessels containing 0, 0.22, 1.0 and 10.0 mg/l of the test material.
Result	:	Exposure to 10.0 mg/l of the test material resulted in 100% mortality at 48 hours. No deaths were observed in the control group and in the groups exposed to other concentrations of the test material. All fish exposed to the test material as well as the untreated controls were normal throughout the study period, except those exposed to 4.6 mg/l which were hyperactive at the 24 hr reading. The 96-hr median lethal concentration (LC50) of Dowfax* Dry Hydrotrope Powder was 6.8 mg/l. Analysis confirmed that the measured test concentration found at 0 and 96 hours were in agreement with the nominal concentrations. The LC50 calculation was therefore based on the nominal concentrations.
Test condition	:	After aeration the hardness of the test medium was 250 mg CaCO3/l and the pH was 8.1.
Test substance	:	The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

15.08.2002 (18)

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	yes
LC50	:	= 13 (calculated)
Method	:	
Year	:	1984
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The method was based on the Dow Environmental Sciences Research Laboratory Standard Operating Procedures for daphnid and fish toxicity tests which were based on procedures recommended by the ASTM Subcommittee on Safety to Aquatic Organisms (1980). This test consisted of exposing groups of 10 fathead minnows to seven concentrations of the test material (32, 24, 18, 13, 10, 7.5, 5.6 mg/L) and a dilution water control. Exposure was initiated by adding appropriate

amounts of an aqueous stock solution of Dowfax C6 to exposure vessels containing 8 L of dilution water and 10 fish. Additional dilution water was simultaneously added to each vessel to aid in mixing of the test solution, bringing the final test volume to 10L. The D.O., pH and temperature were measured daily in representative tanks as long as fish survived. Fish were not fed during the test. Dead fish were removed daily. The LC50 was calculated by probit analysis.

Remark : The LC50 was 13 mg/l with 95% C. I. of 12-14 mg/l.

Result : Water Quality Measurements:

Temperature Range	16.6-16.9 C
pH Range	7.4-8.0
Dissolved Oxygen	
(0-48 hour)	>60% of saturation
(48-96 hour)	>54% of saturation

Raw Data:

32 mg/l	100 % dead 24 hr
24	100 % dead 48 hr
18	100 % dead 48 hr
13	50 % dead 96 hr
10	0 % dead 96 hr
7.5	0 % dead 96 hr
5.6	0 % dead 96 hr

Test substance : The test material was Dowfax C6 surfactant, containing 47.5% active ingredient in water.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

15.08.2002 (19)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : yes
NOEC : = 5.6 (calculated)
EC50 : = 11.8 (calculated)
EC100 :
= 32 (measured)
Method : other: OECD 202 and EEC C.2
Year : 1998
GLP : yes
Test substance : other TS
Method : Subsequent to a range-finding study, 2 replicate groups of 10 daphnia were exposed to aqueous solutions of the test material at nominal concentrations of 5.6, 10, 18, 32, 56 and 100 mg/l. Additional duplicate groups of 10 daphnia were included as untreated controls. The daphnia were exposed under static conditions in 100 ml glass beakers that contained 80 ml of the test medium. The daphnia were observed for immobilization at 24 and 48 hours of exposure. Oxygen concentration and pH of the test solutions were monitored at 0 and 48 hours. Samples were taken at 0 and 72 hours from test vessels containing 0, 5.6, 18 and 100 mg/l test material to verify the nominal test concentrations.

Result : Exposure over 48 hours to the test material resulted in 100% immobilization of the daphnia at the three highest test concentrations (32, 56 and 100 mg/l). 85 and 35% immobilization was observed in the 18 and 10 mg/l vessels, respectively. Exposure to the untreated control solutions and to 5.6 mg/l of the test material did not show any adverse effects.

The nominal 48-hour median effective concentration (EC50) of Dowfax* Dry Hydrotrope Powder in Daphnia magna was 11.8 mg/l (95% c.l. 10.5 and 13.9 mg/l). The experimentally determined No-Observed-Effect Concentration (NOEC) was 5.6 mg/l. 100% immobilization was reached at 32 mg/l. The analytical results confirmed that measured test concentrations were within 80% of the nominal ones. Therefore, the calculation of the EC50 was based on the latter.

Test condition : Hardness of the M7 Medium was 250 mg/l (as CaCO3) and the pH was 8.0 after aeration.
The temperature of the test medium measured in the blank control varied from 20.5 to 20.7C.
The pH at O hr ranged from 8.0-8.2 and at 48 hr from 7.8-8.0.
Dissolved oxygen was 9.2-9.3 at 0 hrs and 8.8-9.0 at 48 hrs.

Test substance : The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
15.08.2002 (20)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : yes
LC50 : = 47 (calculated)
Method :
Year : 1984
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : This test consisted of exposing groups of 10 first instar daphnids to five concentrations of the test material (100, 56, 32, 18, 10 mg/L) and a dilution water control. The 5 test concentrations and the control were set in triplicate. In addition, a fourth beaker was set at the high, middle, low and control concentrations for the purpose of taking daily D.O., pH and temperature measurements. Test concentrations were prepared by adding appropriate amounts of an aqueous stock solution of Dowfax C6 to the test vessels and bringing the final volume up to 200 ml with additional daphnid dilution water. The daphnids were then added to the test vessels. The test organisms were not fed during the test. The LC50 was calculated using probit analysis.
Remark : The LC50 was 47 mg/l with 95% C.I. of 36-64 mg/l at 48 hr.
Result : Water Quality Measurements

Temperature Range	20.0-20.6 C
pH Range	7.9-8.2
Dissolved Oxygen	>111% of saturation

Raw Data:

100 mg/l	77% dead in 48 hr
56	50% dead in 48 hr
32	37% dead in 48 hr
18	30% dead in 48 hr
10	3% dead in 48 hr

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
15.08.2002 (19)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint : growth rate
Exposure period : 72 hour(s)

Unit	:	mg/l
Analytical monitoring	:	yes
NOEC--growth inhibition	:	= 10 (calculated)
NOEC--growth rate reduction	:	= 22 (calculated)
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	Subsequent to a range-finding study the cells of S. capricornutum were exposed to 3 parallel samples of an aqueous nutrient solution (100 ml) containing 10, 22, 46, 100 and 220 mg/l of the test material over a period of 72 hours. Additional six parallel samples were included as blank controls without addition of test substance. The incubation took place on a laboratory shaker at 22.5-23.0C under continuous illumination (7500-8000 lux). Samples of the algae suspensions were taken at 0, 24, 48 and 72 hours and the cell number was determined with the use of a spectrophotometer at 720 nm. As growth parameters the area under the growth curve was determined (used as a base for the calculation of the concentration leading to 50% growth inhibition (EbC50) as well as the growth rate between 0 and 72 hours to calculate the ErC50 (0-72h) value. pH was determined at 0 and 72 hours whereas the temperature was recorded daily. Samples were taken at 0 and 72 hours from test vessels containing 0, 10 and 46 mg/l test material to verify the nominal test concentrations.
Result	:	The nominal effective 72-hour EbC50/ErC50 (0-72h) values of Dowfax* Dry Hydrotrope Powder when tested with S. capricornutum were determined to be 55 mg/;l (95% c.l. 31.6-95.5) and >220 mg/l, respectively. The 72-hour No-Observed-Effect Concentration (NOEC) corresponded to values of 10.0 mg/l (growth inhibition) and 22 mg/l (growth rate reduction). The analytical results confirmed that measured test concentrations were within 80% of the nominal ones. Therefore the calculation of the EC50 values was based on the latter.
Test condition	:	The ISO medium contained 0.24 mmol/l (Ca + Mg) =24 mg CaCO3/l. The temperature fo the test medium ranged from 22.5 to 23.0C. The pH at 0 hr was either 8.3 or 8.2 (top 2 doses) in the vessels and ranged from 7.8 to 8.2 in the various vessels at 72 hr.
Test substance	:	The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

15.08.2002 (21)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	activated sludge of a predominantly domestic sewage
Exposure period	:	30 minute(s)
Unit	:	mg/l
Analytical monitoring	:	no
EC0	:	> 100 (measured/nominal)
Method	:	OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	The effect of the test material on the respiration rate of activated sludge from a municipal waste water treatment plant was determined by comparing the oxygen consumption of two parallel samples treated with 100 mg/l of the test material with two untreated control samples (oxygen determination at the start and end of the experiment). The oxygen

consumption was measured with an oxygen electrode after an incubation period of 30 minutes at 20C. The susceptibility of the activated sludge was evaluated by the addition of 3,5-dichlorophenol (3.2, 10.0 and 32.0 mg/l).

Result : The test substance at a concentration of 100 mg/l showed no significant inhibitory effect on aerobic waste water bacteria. The control with 3,5-dichlorophenol showed an EC50 of 9 mg/l indicating suitability of the test conditions.

Test condition : Test solutions were prepared in 'Milli-Q water'. The pH of the stock solution was 7.5. The pH of the synthetic sewage was 7.0. The temperature of the test medium varied between 19 and 20C. The mean respiration rates of the contols and the EC50 of the reference met the criteria for acceptability of the test.

Test substance : The test was conducted on Dowfax* Dry Hydrotrope Powder.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

15.08.2002 (22)

4.5.1 CHRONIC TOXICITY TO FISH

Reliability : (2) valid with restrictions

14.08.2001

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	Fischer 344
Sex	:	male
Number of animals	:	3
Vehicle	:	
Value	:	> 2000 mg/kg bw
Method	:	
Year	:	1995
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	This study was for industrial product handling and MSDS purposes. The test material was administered undiluted--as sold.
Result	:	All 3 rats survived the 14 day observation period. There was no obvious effect noted.
Test substance	:	The test substance was Dowfax C6L
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

24.04.2002 (23)

Type	:	LD50
Species	:	rat
Strain	:	Fischer 344
Sex	:	male
Number of animals	:	3
Vehicle	:	
Value	:	> 5000 mg/kg bw
Method	:	other
Year	:	1985
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Three rats per dose. The test material was C6 Dowfax. Doses were 1300, 2500 and 5000 mg/kg. The test material was administered undiluted.
Result	:	Transient diarrhea, lethargy and palpebral closure were observed in all rats following dosing. All rats survived the 2-week observation period and steadily gained weight during that period.
Reliability	:	(2) valid with restrictions

24.04.2002 (24)

Type	:	LD50
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	3
Vehicle	:	water
Value	:	> 2000 mg/kg bw
Method	:	Directive 84/449/EEC, B.1 "Acute toxicity (oral)"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	Three male and three female fasted Wistar rats were given a single oral dose of the test material in water at a dose of 2000 mg/kg (10 ml/kg). Animals were observed at 0, 2 and 4 hours after dosing and then once daily for 15 days. Individual body weights were recorded on the day of treatment and on days 8 and 15. Animals were examined for gross pathological changes at the termination of the study.
Result	:	There were no deaths. Diarrhea was noted in all males on day 1.

Salivatiion and rales were observed in one female on day 1 and 2, respectively. No other treatment related advese effects were noted. All animals showed the expected body weight gain during the study. No abnormalities were noted at necropsy. Thus, the acute oral median lethal dose (LD50) of Dowfax* Dry Hydrotrope Powder was >2000 mg/kg body weight in the Wistar rat.

Test substance : The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
24.04.2002 (25)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Species : rat
Strain : Wistar
Sex : male/female
Number of animals : 5
Vehicle : water
Value : > 2000 mg/kg bw
Method : OECD Guide-line 402 "Acute dermal Toxicity"
Year : 1998
GLP : yes
Test substance : other TS
Method : Five male and five female Wistar rats were treated with a single, occluded, dermal application of the test material mixed with water at a concentration of 20% (W/w). The dose volume was 10 ml/kg. The material was applied at a dose of 2000 mg/kg body weight to an area of shorn skin which approximated 10% of the total body surface area. Twenty-four hours after application, the dressing and residual test material were removed. The rats were observed for signs of toxicity and death at 0, 2 and 4 hours after dosing and subsequently once daily for 15 days. Body weights were recorded on the day of treatment and on days 8 and 15. The rats also were examined for gross pathologic changes at the termination of the study.
Result : Dermal application of the test material did not result in any deaths. No clinical signs of systemic toxicity were noted during the study. Adverse skin reactions at the treatment sites included necrosis developing into scabs in all females and one male. The effects had resolved between days 7 and 9. No significant effects on body weight were noted during the study and there were no treatment related post-mortem observations at the termination of the study.

The acute, dermal, median lethal dose (LD50) of Dowfax* Dry Hydrotrope Powder in Wistar rats was >2000 mg/kg body weight.

Test substance : The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
24.04.2002 (26)

Type : LD50
Species : rabbit
Strain : New Zealand white
Sex : female
Number of animals : 2
Vehicle :

Value	:	> 2000 mg/kg bw
Method	:	other
Year	:	1985
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Two rabbits were treated with 2000 mg/kg of the undiluted test material. The material was placed under a plastic cuff which was secured by rubber bands and then wrapped with a cotton cloth. After 24 hours, the wrappings were removed and the site washed with water and signs of irritation recorded. The rabbit was observed for behavioral changes as indicators of toxicity up to removal of the test material and for the subsequent 2 weeks. The rabbits were weighed on days 0, 1, 7 and 14.
Result	:	Slight redness and swelling was observed on the application sites of rabbits 24 hours following exposure. Transient lethargy was observed following treatment. Both rabbits steadily gained weight during the 2-week test period.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

24.04.2002 (24)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	
Exposure time	:	
Number of animals	:	1
PDII	:	
Result	:	slightly irritating
EC classification	:	not irritating
Method	:	other
Year	:	1995
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The 'neat' Dowfax C6L was applied to the inner surfact of the left ear and to intact and abraded skin on the abdomen of one male NZ white rabbit. Five consecutive applications were made to the ear and the intact abdominal site. Three consecutive applications were made to the abraded abdominal site. The abdominal sites were covered with cotton wool and wrapped in cotton cloth secured with tape to the marginal fur. This is a 'range-finding' type test conducted for handling and MSDS purposes.
Result	:	No clinical signs indicative of systemic toxicity were observed. Very slight erythema was observed at the ear application site. Very slight to slight erythema was observed at the abdominal test sites. Erythema at all application sites may have been due to mechanical damage which occurred during test material removal. Very slight edema was observed at the intact abdominal application site, after five applications. Dermal application of Dowfax C6L had no effect on body weight.
Reliability	:	(2) valid with restrictions

24.04.2002 (23)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	
Exposure time	:	
Number of animals	:	1

PDII	:	
Result	:	not irritating
EC classification	:	not irritating
Method	:	other
Year	:	1985
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The undiluted C6 Dowfax was applied to the ear of one New Zealand white rabbit for 10 consecutive weekdays; to an intact site on the abdomen for 10 consecutive weekdays; and to an abraded site on the abdomen for 3 consecutive days. The ear site was left uncovered; the abdominal sites were covered with cotton wool and then cotton cloth which was taped to the marginal skin. The rabbits were observed for the first 11 days on test and then at day 14. Body weights were taken at days 0, 7 and 14.
Result	:	There was no irritation observed at any site at any observation time. There was no indication of systemic toxicity observed by behavior nor body weight parameters.
Reliability	:	(2) valid with restrictions

24.04.2002 (24)

Species	:	rabbit
Concentration	:	other: moistened with water
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	3
PDII	:	
Result	:	slightly irritating
EC classification	:	not irritating
Method	:	Directive 84/449/EEC, B.4 "Acute toxicity (skin irritation)"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	Three rabbits were exposed to 0.5 g of Dowfax* Dry Hydrotrope Powder, applied onto cliped skin (moistened with water) for 4 hours using a semi-occlusive dressing. Observations were made 1, 24, 48 and 72 hours after exposure.
Result	:	Exposure to Dowfax* Dry Hydrotrope Powder resulted in very slight to well-defined erythema with or without very slight edema in the treated skin areas of the three rabbits. The skin irritation had resolved within 48 hours after exposure in all animals.
Test substance	:	The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

24.04.2002 (27)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	
Exposure Time	:	
Comment	:	
Number of animals	:	1
Result	:	moderately irritating
EC classification	:	irritating
Method	:	other
Year	:	1995
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The 'neat' Dowfax C6L was instilled (0.1ml) into each conjunctival sac of a

male New Zealand White rabbit. One eye was washed with water after a 30-second exposure, while the other eye was washed with water after one hour. Moderate discomfort was exhibited by the animal immediately after instillation of the test material, in the first eye dosed. Ophthaine ocular anesthetic was then instilled into this eye and into the other eye prior to test material instillation. Observations were made at 24, 48 72 hrs and at one week.

Result : Moderate to severe conjunctival redness and swelling was observed in both eyes from immediately afte dosing through the 72 hour read. The 30-second exposure eye had very slight irritation of the iris immediately after dosing, and both eyes had very slight to moderate irritation of the iris from one hour after dosing through the 48 hour read. The one hour wash exposure eye had slight corneal opacity after staining with fluorescein, at the one hour read. Both eyes had very slight corneal opacity before staining and very slight to moderate corneal opacity after staining with fluorescein from the 24 hour read through the 72 hour read. Ocular irritation was resolved by seven days after dosing and the test was terminated.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
24.04.2002 (23)

Species : rabbit
Concentration : undiluted
Dose :
Exposure Time :
Comment :
Number of animals : 1
Result : moderately irritating
EC classification : irritating
Method : other
Year : 1985
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : Undiluted C6 Dowfax was instilled into each conjunctival sac of a female New Zealand White rabbit. One eye was washed after 30 seconds and the other after one hour. Observations were made after 24, 48, 72 hrs and after 7, 14 and 21 days.

Result : Instillation of C6 Dowfax resulted in moderate discomfort, marked conjunctival redness and swelling, moderate reddening of the iris and moderate corneal haziness. All signs of irritation were essentially resolved in the unwashed eye 7 days post-exposure. In the eye which was treated and subsequently washed, signs of irritation were still exhibited 21 days post-exposure.

Reliability : (2) valid with restrictions
Flag : Material Safety Dataset
24.04.2002 (24)

Species : rabbit
Concentration : 5 %
Dose : .1 ml
Exposure Time : 24 hour(s)
Comment :
Number of animals : 6
Result : slightly irritating
EC classification : not irritating
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1998
GLP : yes
Test substance : other TS
Method : An ocular anesthetic was used for all rabbits after discomfort was observed in the first rabbit dosed.

Result	:	Slight conjunctival redness was present in the treated eyes of all rabbits one hour after dosing. Two of the rabbits had slight chemosis, three rabbits had slight ocular discharge, and two rabbits had reddening of the iris one hour after dosing, as well. Twenty-four hours after dosing, all rabbits had slight conjunctival redness, five rabbits had slight chemosis, one rabbit had slight ocular discharge, three rabbits had opacity of the cornea, and one rabbit had reddening of the iris. Forty-eight hours after dosing, three rabbits had slight conjunctival redness, three rabbits had slight chemosis, and three rabbits had opacity of the cornea. The ocular lesions were resolved in all animals 72 hours after instillation of the test material, and the test was terminated. Instillation of 5% aqueous Dowfax C6L into the eye had no effect on body weight of rabbits. The average combined scores for 24, 48 and 72 hours were: Redness: 0.5 Chemosis: 0.444 Corneal Opacity: 0.333 Reddening of the Iris: 0.06
Test substance	:	The test material was a 5% aqueous solution of Dowfax C6L. This is the use dilution.
Reliability	:	(1) valid without restriction
Flag	:	Material Safety Dataset
24.04.2002		(28)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	33 other: mg
Exposure Time	:	
Comment	:	not rinsed
Number of animals	:	3
Result	:	highly irritating
EC classification	:	irritating
Method	:	Directive 84/449/EEC, B.5 "Acute toxicity (eye irritation)"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	Single samples of 33 mg of Dowfax* Dry Hydrotrope Powder were instilled into one eay of each of three rabbits. Observations were made 1, 24, 48, and 72 hours and 6, 7, 14 and 21 days after instillation.
Result	:	Instillation of Dowfax* Dry Hydrotrope Powder resulted in adverse effects on the cornea, iris and conjunctivae. Corneal injury consisted of opacity (maximum grades 1 and 2) and epithelial damage (maximum 35 to 100% of the corneal area). Neovascularization was apparent in one animal 7 and 14 days after instillation. The corneal injury had completely resolved within 7 to 21 days. Iridic irritation (grade 1) was observed in all animals and had resolved within 48 hours. The irritation of the conjunctivae consisted of redness, chemosis and discharge and had completely resolved within 14 days in all animals.
Test substance	:	The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
24.04.2002		(29)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	Induction 1 % intracutaneous

Induction 50 % occlusive epicutaneous
Challenge 50 % occlusive epicutaneous

Number of animals	:	10
Vehicle	:	water
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	other: OECD 406 and EC B.6
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	The concentration of the test material used in the main study was based on the results of a pretest. Ten test and five control female Dunkin-Hartley guinea pigs were used for the main study. Intradermal induction consisted of two injections (0.1 ml per site) of the test material (1.0% w/v in water), with and without Freund's Complete Adjuvant, and a control with Adjuvant alone. After one week, the scapular area between the two intradermal injection sites (one day before the topical treatment the skin was rubbed with 10% (w/v) sodium dodecyl sulfate to increase sensitivity) was treated topically for 48 hours with 0.5 ml of a 50% (w/v) dilution of the test material in water. Induction readings were made at day 3 (after intradermal injection) and day 10 (after epidermal exposure). Chalenge on day 21 consisted of a single, 24-hour, topical application (0.5 ml) fo the test material at a concentration of 50% w/v in water on one flank of each test and control animal under an occlusive dressing. Observations for any dermal reaction were made approximately 24 and 48 hours after removal of the dressing.
Result	:	The induction readings were: on day 3 (after intradermal injection)--well-defined to moderate erythema (controls) and severe erythema with cases of necrosis (experimental animals); on day 10 (after epidermal exposure)--no adverse effects to slight erythema with small scabs (control and experimental animals). Generally, no edema was observed. No signs of skin reactions were evident after the challenge exposure in the experimental and control animals.
Test substance	:	The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

24.04.2002 (30)

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	other
Route of admin.	:	gavage
Exposure period	:	28 consecutive days
Frequency of treatment	:	daily
Post obs. period	:	None
Doses	:	targeted 0, 50, 250 or 1000 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL	:	= 50 mg/kg
LOAEL	:	= 250 mg/kg
Method	:	OECD Guide-line 407 "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-d Study"
Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of 5 male and female CD rats were given Dowfax XD 8292 by oral gavage at doses of 0, 50, 250 or 1000 mg/kg/day for 28 consecutive days.

Parameters examined were daily clinical observations, weekly food consumption, water consumption by inspection, twice weekly body weights, calculated food conversion ratios, hematology (PCV, Hb, RBC, WBC, platelets, differentials, MCHC, MCV and MCH) and blood chemistry (AP, ALT, AST, urea, creatinine, glucose, bilirubin, total protein conc., electrophoretic protein fractions, Na, K)at 3 weeks, urinalysis at 3 weeks (appearance, volume, pH, sp.gr., protein, total reducing substances, glucose, ketones, bilirubin, urobilin, nitrite, blood, sed.), macroscopic examination, organ weights (adrenals, heart, kidneys, liver, spleen, testes), microscopic exams of adrenals, heart, kidneys, liver, spleen, stomach and macroscopically abnormal tissues.

Data were examined by various appropriate statistical methods.

Remark : The rats were CD rats (remote Sprague-Dawley origin).
The stomach irritation seen in females at 250 mg/kg/day was judged to be of questionable toxicologic significance by these authors.

Result : There were no adverse effects on body weights, food consumption or food utilization during the course of the study. However, post-dosing salivation was observed throughout the study in the group given 1000 mg/kg/day. There were also several minor changes in clinical chemistry parameters and urinalyses for animals in the high dose group; changes in some of these parameters also occurred in animals in the 250 mg/kg/day group. At necropsy, there were no differences in organ weights nor any macro pathological changes clearly attributable to treatment with the test material. Histopathological examinations revealed acute inflammation of the glandular gastric mucosa of all animals treated at 1000 mg/kg/day, as well as in females given 250 mg/kg/day. There were no treatment-related effects in either male or female rats given 50 mg/kg/day.

Source : Life Sciences Research, Suffolk, England for Dow Chemical Europe.

Test substance : The test material was Dowfax* XD 8292 (primarily C-6 alkylated sodium sulfonated diphenyl oxide), 45.8% active ingredient. Doses cited in the report are expressed gravimetrically in terms of the active component (45%, assumed w/v).

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

24.04.2002 (31)

Species : rat
Sex : female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : 10 consecutive days
Frequency of treatment : daily
Post obs. period : None
Doses : 10
Control group : yes, concurrent vehicle
NOAEL : = 367 mg/kg bw
LOAEL : = 1223 mg/kg bw
Method : other
Year : 1985
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : This study was conducted for the purpose of dose-setting for the Chernoff test which was required for the PMN.

Groups of 10 adult female F-344 rats were given Dowfax C-6 alkylate sodium sulfonate in water by gavage for 10 consecutive days with dose levels targeted at 0, 100, 300 and 1000 mg/kg bw/day. The top dose was selected on the basis of the regulatory guidelines for the Chernoff test which require a dose level sufficiently high to produce overt maternal toxicity, to a maximum dose of 1000 mg/kg/day. The low and middle dose

levels were selected as approximate half-log decrements of the high dose level. Analysis of dosing solutions revealed actual dose levels to be 122, 367 and 1223 mg/kg/day. Rats were dosed at a volume of 4 ml/kg/day, with dose volumes adjusted daily according to body weights.

Feed and water consumption were recorded at 3-day intervals during the dosing period. Animals were observed at least once daily throughout the dosing period for signs of toxicity. Animals found moribund were submitted for gross pathologic examination.

At termination, a complete necropsy examination, external and internal, was performed by a veterinary pathologist. Terminal body weights and weights of the liver, kidneys, brain, heart and thymus were recorded at the time of necropsy. The eyes were examined in situ by gently pressing a glass slide against the cornea and observing the eyes under fluorescent light illumination. Tissues routinely collected (44) were saved from all animals in neutral phosphate buffered 10% formalin; however, histologic examination was not deemed necessary.

Results were examined by a variety of appropriate statistical methods.

Result : At 1223 mg/kg/day, rats exhibited clinical signs of loose/watery stools with perineal staining. Necropsy examination of these animals revealed gas and watery ingesta in the gastrointestinal tract. Increased absolute and relative liver weights and decreased absolute and relative thymic weights were observed in rats given 1223 mg/kg/day when compared to controls. Relative liver weight increases at 122 and 367 mg/kg/day were considered secondary to the apparent incidental decreases in weight gain in these two groups (control weight gains at high end of historical range).

Conclusion : Based on the results of this study, doses of 1000 and 300 mg/kg/day would be used for the proposed Chernoff study.

Reliability : (2) valid with restrictions

Flag : Material Safety Dataset

24.04.2002 (32)

Type : Sub-acute
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : 14 days
Frequency of treatm. : daily
Post exposure period :
Doses : 0, 20.8, 125, 625 and 2083 mg/kg/day corresponding to 0, 9, 54, 271 and 904 mg/kg/day active ingredient
Control group :
Method :
Year :
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : This range-finding study was designed to select dose levels for an OECD 421 (Reproduction/developmental toxicity screening test). Due to observations in an OECD 421 study using Dowfax 8390, a higher MW material in this category, a coagulation parameter, prothrombin time, was measured.

Groups of 5 male and 5 female rats were dosed orally with 0, 20.8, 125, 625 or 2083 mg/kg/day Dowfax C6L. These dose levels corresponded to targeted active dose levels of 0, 9, 54, 271 or 904 mg/kg/day, respectively. A detailed clinical examination was performed daily approximately 30-90 minutes after dosing. Body weight and feed consumption were measured weekly. The day after the last dose, blood samples were obtained to

measure prothrombin times. Body, kidney and liver weights were measured and a gross examination was conducted on each rat.

Statistical Analysis: For sample sizes for groups of 3 or greater, Levene's test was used to assess homogeneity of group variances for each specified endpoint and for all collection intervals. If Levene's test was not significant ($p>0.01$), a pooled estimate of the variance was computed from a one-way analysis of variance and utilized by a Dunnett's comparison of each treatment group with the control group. If Levene's test was significant ($p<0.01$), comparisons with the control group were made using Welch's t-test with a Bonferroni correction.

Result : All animals survived to the scheduled necropsy. There were no consistent treatment-related clinical observations during the 14 day dosing period. Body weight and feed consumption for all groups administered Dowfax C6L were comparable to control values. Mean prothrombin time was decreased slightly (8%) from control values in females administered 2083 mg/kg/day Dowfax C6L. This decrease was not considered toxicologically significant. At necropsy, one male rat exhibited a mild, red discoloration of the lung. This was only noted in the left diaphragmatic pulmonary lobe and was not considered to be toxicologically significant. All other animals appeared to be normal. The mean relative kidney weight of females in the 2083 mg/kg/day group was statistically increased from control values. The absolute kidney weight was also increased, albeit not statistically. All other mean kidney and liver weight values were comparable to control values.

Test substance : Dowfax C6L was determined to contain 50.66% water using Karl Fischer volumetric titration. The purity of the sample was found to be (by difference) 43.4% using ion chromatography and Neutron Activation Analysis. Infrared spectroscopy (FTIR) and liquid chromatographic mass spectroscopy (LC/MS) were used to confirm the proposed structure of Dowfax C6L.

Conclusion : Based on the results of this two-week range finding study, dose levels of 0, 60, 200 and 1000 mg/kg/day active ingredient (based on 43.3% purity) will be used for the OECD 421 study.

24.05.2006 (33)

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : at least 42 days for males and up to 54 days for females
Frequency of treatm. : daily
Post exposure period :
Doses : 60, 200 and 1000 mg/kg/day active ingredient corresponds to 125, 417 and 2083 mg/kg/day Dowfax C6L
Control group : yes, concurrent vehicle
Method : other: OECD 421
Year :
GLP : yes
Test substance :

Method : Groups of 12 male and 12 female Sprague Dawley rats were administered 0, 60, 200 or 1000 mg/kg/day active ingredient (corresponding to 0, 125, 417 or 2083 mg/kg/day Dowfax C6L respectively). The vehicle, distilled water, was administered at a dose volume of 4 ml/kg. Animals were observed daily for clinical signs. Body weights and feed consumption were obtained during the premating, gestation, lactation and post-mating periods. After two weeks of vehicle or test material administration, the females were cohabitated with males, one male to one female, from the same treatment group, for up to 14 days. Vaginal smears were evaluated daily in females during the 14-day period to establish estrous cyclicity. Once mating was confirmed on gestation day 0 (GD 0), females were

separated from the male for the remainder of gestation and allowed to deliver and nurse litters until lactation day (LD) 4. Observations of the F1 pups included survival at birth and during lactation, individual pup body weights and sex, and clinical examinations on LD0 and 4. Complete necropsies were performed on all adult animals. At necropsy, terminal body weights as well as kidney and liver weights were obtained, In addition, testes and epididymides weights were obtained from all males. The following tissues were examined microscopically: kidney, liver and pituitary gland from all animals. In addition, epididymides, prostate, seminal vesicles w/coagulating glands and testes were examined from males and mammary gland, ovaries, oviducts, uterus with cervix and vagina were examined from females. Pups that survived to scheduled euthanasia (LD4) were examined externally and subjected to a complete gross necropsy.

Statistical analysis:
Group Pair-Wise Comparisons - For sample sizes for groups of 3 or greater, Levene's test was used to assess homogeneity of group variances for each specified endpoint and for all collection intervals. If Levene's test was not significant ($p>0.01$), a pooled estimate of the variance was computed from a one-way analysis of variance and utilized by a Dunnett's comparison of each treatment group with the control group. If Levene's test was significant ($p<0.01$), comparisons with the control group were made using Welch's t-test with a Bonferroni correction.
Arcsin-Square-Root Transformation - Data comprised of percent values were transformed using the arcsin of the square root. The analysis described in the Group Pair-wise Comparisons section was then used to analyze the transformed percentage values.
Fisher's Exact Test - An overall test for association between response and treatment was conducted using a Fisher's exact test. If this overall test was significant ($p<0.05$) and there were more than two groups, then a follow up analysis was done, where each treatment group was compared to the control group using a Fisher's exact test.
Covariate Analysis - For the mean of pup body weights per dam and time period, an analysis of covariance using litter size as a covariate was conducted to compare treatment groups. Each treatment was compared to control using Dunnett's test under the analysis of covariance model.

Results were reported at the 0.05 and 0.01 significance levels. All endpoints were analyzed using two-tailed test.

Result : Two males and four females in the high dose group died during the course of the study. The males died on study days 49 and 57 while the females died on premating day 4, GD16, LD1 and LD3. These effects were considered to be test material related.

Decreased activity, salivation, soft and watery feces, audible and difficult breathing were observed in the high dose male rats. Most of the clinical observations were related to the animals that died. During the premating, gestation and lactation period, similar clinical findings were observed in the high dose female rats but with a lower frequency.

Mean body weights of treated male rats were comparable to control values throughout the study (Table 1). Mean body weight gain of the high dose male rats was statistically significantly decreased during the first two weeks of premating. A slight decrease was noted at the end of the study in the high dose male rats.

Mean body weights of treated female rats were comparable to control values throughout the study (Table 2). Body weight changes in females were significantly decreased in the high dose group (1000 mg/kg/day) at GD interval 14-20. The decrease in body weight was considered to be

treatment-related. During lactation, body weight changes in low dose female rats was significantly decreased from control values. This was not observed in female rats dosed at 200 or 1000 mg/kg/day. This was considered to not be treatment-related since there was no dose-response relationship and mean body weight values were comparable to control values.

Feed consumption was comparable between male groups. In female rats, feed consumption in the groups administered test material was not significantly decreased in the premating and gestation periods. In the low dose group, female rats had a statistically significant decrease during laction which correlated with the body weight change.

Mean estrous cycle length and number of estrous cycles were comparable among the groups, including control.

There were no treatment-related organ weight changes noted in rats of either sex.

At necropsy, there were no treatment-related gross pathologic observations. One animal that died during the study had discolored liver which corresponded microscopically with minimal focal necrosis. This finding was not noted in any other animal at scheduled necropsy. All other macroscopic and microscopic changes were typical of those commonly observed in rats of the same stain and age and were considered to be incidental.

Reproductive Performance:
There were no test material related changes in mating, fertility and fecundity indices in male and female rats. The copulatory interval was increased slightly in the high dose group, but the value (3.8 days) was within the historical control range of 2 to 4.8 days.

Gestation length and gestation index, number of pups born per litter, number of dead pups, stillborn index, and total implantation scars per litter were not affected. On LD4, pup sex ratio and mean number of live pups/litter were comparable among the groups. The pup viability index for the high dose animals was slightly decreased at 85.9%, as compared to the control value of 97.2%.

Several pups in the high dose group were observed with decreased activity and cold to the touch. Each observation was observed in ten or less pups on LD0 and only one pup was cold to the touch on day 4. Pup body weight by sex and both sexes combined was significantly reduced in the high dose group on LD0. Similarly, on LD4, male pup body weights and both sexes combined were significantly reduced in the high dose group. However, female pup body weight on LD4 was decreased but not significantly. There were no grossly visible lesions observed in either sex on LD4.

Test substance : Dowfax C6L was determined to contain 50.66% water using Karl Fischer volumetric titration. The purity of the sample was found to be (by difference) 43.4% using ion chromatography and Neutron Activation Analysis. Infrared spectroscopy (FTIR) and liquid chromatographic mass spectroscopy (LC/MS) were used to confirm the proposed structure of Dowfax C6L.

Attached document : Table 1

An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 5 **Summary of Body Weight Values - MALE**

Endpoint	Study Interval (Week)	0 mg/kg/day (Vehicle Control) Mean	SD	N	60 mg/kg/day Mean	SD	N	200 mg/kg/day Mean	SD	N	1000 mg/kg/day Mean	SD	N
Body Weight Values g													
Premating	1	287.9	10.77	12	287.8	8.85	12	286.9	9.01	12	287.4	10.41	12
	2	323.6	14.76	12	327.5	13.24	12	316.7	13.28	12	311.0	21.80	12
Pairing	3	356.3	22.46	12	364.8	18.92	12	347.3	21.93	12	341.8	31.39	12
	4	385.2	29.95	12	390.2	23.08	12	374.3	30.76	12	366.1	20.88	12
Postmating	5	413.4	32.25	12	425.2	25.83	12	406.9	32.76	12	396.0	25.09	12
	6	440.8	36.74	12	452.3	26.00	12	432.4	35.85	12	419.6	28.46	12
	7	448.5	32.27	12	463.1	29.16	12	439.8	35.09	12	429.8	32.97	12
	8	465.2	32.65	12	477.2	29.94	12	454.2	38.53	12	447.4	32.94	11
	9	483.3	36.61	12	498.3	31.16	12	473.9	37.65	12	458.5	43.11	11

Attached document : Table 2

An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 6 **Summary of Premating Body Weight Values - FEMALE**

Endpoint	Study Interval (Week)	0 mg/kg/day (Vehicle Control) Mean	SD	N	60 mg/kg/day Mean	SD	N	200 mg/kg/day Mean	SD	N	1000 mg/kg/day Mean	SD	N
Body Weight Values g													
	1	220.3	9.91	12	220.1	5.90	12	220.9	9.82	12	222.7	8.50	12
	2	223.2	12.55	12	230.3	9.69	12	230.6	10.46	12	228.0	11.96	11

An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 7 **Summary of Gestation Body Weight Values**

Endpoint	Study Interval (Day)	0 mg/kg/day (Vehicle Control) Mean	SD	N	60 mg/kg/day Mean	SD	N	200 mg/kg/day Mean	SD	N	1000 mg/kg/day Mean	SD	N
Body Weight Values g													
	0	239.5	13.39	12	251.1	9.42	8	244.9	9.08	11	247.2	9.73	9
	7	280.7	16.27	12	289.4	9.44	8	280.4	16.67	11	277.9	12.93	9
	14	312.3	19.45	12	320.0	13.58	8	310.3	18.29	11	305.7	20.35	9
	20	393.7	22.83	12	396.6	26.79	8	391.1	20.11	11	378.6	22.52	8

An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 8 **Summary of Lactation Body Weight Values**

Endpoint	Study Interval (Day)	0 mg/kg/day (Vehicle Control) Mean	SD	N	60 mg/kg/day Mean	SD	N	200 mg/kg/day Mean	SD	N	1000 mg/kg/day Mean	SD	N
Body Weight Values g													
	0	287.8	22.11	12	304.0	13.36	11	297.5	15.28	12	274.5	23.49	10
	4	304.8	18.30	12	305.5	15.61	11	307.0	22.15	12	296.9	16.18	8

Conclusion : Mortality and clinical signs of toxicity were observed in parental animals from the high dose group, 1000 mg/kg/day. Body weight changes were also affected in the high dose group during gestation. In pups, test material related clinical signs and body weight effects were observed in the high dose group and these findings were observed in conjunction with maternal toxicity. Based on the results of this study, the No-Observed-Effect-Level (NOEL) for maternal and developmental toxicity was considered to be 200 mg/kg/day.

Reliability : (1) valid without restriction
1a: GLP guideline study

05.06.2006 (34)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Dowfax C6L Surfactant was evaluated in the Salmonella-Escherichia coli/mammalian-microsome bacterial mutagenicity assay using a pre-incubation modification of the standard assay.
Concentration : Dowfax C6L Surfactant was evaluated at doses of 100, 250, 500, 1000, 2500 up to a concentration of 5000 micrograms/plate.
Cycotoxic conc. : Above 5000 micrograms/plate
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year : 1996
GLP : yes

Test substance	:	as prescribed by 1.1 - 1.4
Method	:	A range-finding study was used to determine the concentrations for the main study. There was no cytotoxicity in the range-finding study. Tester strains were TA98, TA100, TA1535, TA1537 and Escherichia coli WP2uvrA. The vehicle was DMSO. Positive controls were as prescribed by the guidelines.
Source	:	Corning Hazleton, Vienna, VA, USA for The Dow Chemical Company, Midland, Michigan, USA
Conclusion	:	The test material did not induce a positive increase in the number of revertant colonies in any of the tester strains either in the rpesence or absence of the external metabolic activation system. The results were confirmed in an independent repeat assay. All criteria for a valid study were met.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

24.04.2002 (35)

Type	:	Ames test
System of testing	:	S. typhimurium and E. coli
Concentration	:	6-10,000 micrograms/plate
Cycotoxic conc.	:	6800-10,000 micrograms/plate without and 10,000 micrograms/plate with activation
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: OECD 471 and EEC B.14
Year	:	1999
GLP	:	yes
Test substance	:	other TS
Method	:	The plate incorporation standard procedure with and without the addition of rat liver homogenate as activation system was used in two independent assays. The doses per plate covered a range of 6 to 10,000 micrograms. Besides the number of revertants the possible bactericidal effects were assayed by observing the density of the bacterial background lawn on the plates. Standard positive and solvent controls were included to verify the acceptability of the test conditions, the specific spontaneous mutation frequency of the individual test strains as well as the ability of the rat liver homogenate to metabolically activate the standard promutagens. Tester strains were (TA 1535, TA 1537, TA 100 and TA 98) and WP2uvrA in the case of E. coli. Physiological saline and DMSO were used as solvents for reference substances. A variety of chemicals were used as positive controls, choices taken from recommendations in the published methods.
Result	:	No significant increase in the mutation frequency was seen in any of the bacterial strains at any of the dose levels including the highest concentration tested (10,000 micrograms/plate) with and without activation. All of the positive controls produced a marked increase in mutation frequency in the expected range. No inhibition of the bacterial lawn was observed even at the highest concentrations. However, at concentrations of 6800 - 10,000 micrograms/plate without activation and 10,000 micrograms/plate with activation the number of spontaneous revertants significantly decreased indicating bactericidal effects. Based on these findings Dowfax* Dry Hydrotrope Powder can be considered to be non-mutagenic to the tester strains of Salmonella typhimurium and Escherichia coli used in this study.
Test substance	:	The test substance was Dowfax* Dry Hydrotrope Powder.
Reliability	:	(1) valid without restriction

Flag	:	Critical study for SIDS endpoint
24.04.2002		(36)
Type	:	Chromosomal aberration test
System of testing	:	Cultured peripheral human lymphocytes
Concentration	:	Based on mitotic indices ..... Absence of S-9: 1000, 3330 and 5000 micrograms/ml Presence of S-9: 1000, 3330, and 5000 micrograms/ml
Cycotoxic conc.	:	Absence of S-9: the mitotic index was reduced by 50-60% at doses of 3330 and 5000 micrograms/ml Presence of S-9: the mitotic index was reduced slightly at 1000 and 3330 micrograms/ml but not at 5000 micrograms/m
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Dowfax XD 8292 was tested up to cytotoxic concentrations (5000 micrograms/ml), both in the presence and absence of a metabolic activation system (Aroclor-1254 induced rat liver S9-mix).
Result	:	The test substance induced a statistically significant, dose-related increase in the numbers of cells with chromosome aberrations in the absence of a metabolic system. The types of aberrations induced mainly consisted of simple aberrations (breaks, gaps, fragments). In the presence of S9-mix, statistically significant increases were observed at two doses; however, there was no dose-response relationship. Positive control chemicals, mitomycin C and cyclophosphamide, both produced a statistically significant increase in the incidence of chromosome aberrations. It was concluded that the test substance was clastogenic in human lymphocytes under the conditions of the assay. The authors stated, "The high peroxide content of the test substance (210 ppm)[sic] might have contributed to the observed effect."
Source	:	Notox Toxicological Research & Consultancy C.V., for Dow Europe.
Test substance	:	The test material was a brown liquid containing 205 +/- 20 ppm peroxide. The trade name was Dowfax XD 8292.
Reliability	:	(2) valid with restrictions
Flag	:	Directive 67/548/EEC
24.04.2002		(37)
Type	:	Chromosomal aberration test
System of testing	:	Rat Lymphocytes
Concentration	:	Absence of S-9: 0, 50, 167, and 500 micrograms Dowfax C6L Surfactant per ml of culture medium. Presence of S-9: 0, 167, 500 and 1667 micrograms/ml.
Cycotoxic conc.	:	Mitotic indices were reduced at 1667 micrograms/ml in the absence of S-9 and between 500 adn 1667 micrograms/ml with S-9.
Metabolic activation	:	with and without
Result	:	negative
Method	:	EPA OTS 798.5375
Year	:	2001
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Approximately 48 h after the initiation of whole blood cultures, cells in the absence of S-9 activation were treated for 24 hours with targeted doses of 0, 16.7, 50, 167, 500, 1667 and 5000 micrograms Dowfax C6L Surfactant per ml of culture medium and harvested at the end of treatment. In the presence of S-9 activation, cultures were treated for 4 h and harvested 20 h after treatment termination. Cultures treated with 0.05 and 0.075 micrograms/ml mitomycin C or 4 and 6 micrograms/ml cyclophosphamide were used as positive controls for the non-activation and activation assays, respectively; only one dose level was evaluated for aberrations. Based on

		the mitotic indices, cultures treated with targeted doses of 0, 50, 167 and 500 micrograms/ml in the absence of S-9 activation and cultures treated with targeted doses of 0, 167, 500 and 1667 micrograms/ml in the presence of S-9 activation were selected for determining the incidence of chromosomal aberrations.
Result	:	No significant increase in the incidence of aberrant cells was noticed at any of the treatment levels when compared to the negative controls. The positive control cultures had significantly higher incidences of abnormal cells. Hence, Dowfax C6L surfactant was considered to be negative in the in vitro chromosomal aberration assay using rat lymphocytes.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

24.04.2002 (38)

Type	:	Chromosomal aberration test
System of testing	:	Rat Lymphocytes
Concentration	:	Absence of S-9: 0, 145.2, 290.4 and 387.2 micrograms/ml Presence of S-9: 0, 72.6, 290.4 and 774.4 micrograms/ml
Cycotoxic conc.	:	Absence of S-9: mitotic indices slightly reduced at 387.2 to 484 micrograms/ml Presence of S-9: No change in mitotic indices at top level of 774.4 micrograms/ml
Metabolic activation	:	with and without
Result	:	negative
Method	:	EPA OPPTS 870.5375
Year	:	1998
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	approximately 48 h after the initiation of whole blood cultures, cells in the absence of S-9 activation were treated for 24 hours with targeted doses of 0, 12.1, 36.3, 72.6, 145.2, 217.8, 290.4, 387.2 and 484 micrograms Dowfax Dry Hydrotrope Powder per ml of culture medium and harvested at the end of treatment. In the presence of S-9 activation, cultures were treated for 4 h with dose levels of 0, 36.3, 72.6, 145.2, 290.4, 435.6, 580.8, 677.6 and 774.4 micrograms/ml Dowfax Dry Hydrotrope Powder per ml of culture medium and harvested 20 h after treatment termination. Based upon the mitotic indices, cultures treated with targeted doses of 0, 145.2, 290.4 and 387.2 micrograms/ml in the absence of S-9 activation adn cultures treated with targeted doses of 0, 72.6, 290.4 and 774.4 micrograms/ml in the presence of S-9 activation were selected for determining the incidence of chromosomal aberrations.
Result	:	No significant increase in the incidence of aberrant cells was noticed at any of the treatment levels when compared to the negative controls. Cultures treated with the positive control chemicals (i.e., mitomycin C without S-9 and cyclophosphamide with S-9) had significantly higher incidences of abnormal cells. Hence, Dowfax Dry Hydrotrope Powder was considered to be negative in the in vitro chromosomal aberration assay using rat lymphocytes.
Test substance	:	Benzene, 1,1'-oxybis-, sec-hexyl derivatives, sulfonated sodium salts, a powder having 92% active ingredient.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

24.04.2002 (39)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENITY

5.8.1 TOXICITY TO FERTILITY

Type	:	other
Species	:	rat
Sex	:	female
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	days 6 through 15 of gestation
Frequency of treatment	:	daily
Premating exposure period		
Male	:	None
Female	:	None
Duration of test	:	Day 6 of gestation through day 3 post-partum
Doses	:	0, 300 or 1000 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL Parental	:	< 300 mg/kg bw
NOAEL F1 Offspr.	:	> 1000 mg/kg bw
Method	:	
Year	:	1985
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Chernoff Test: Pregnant female Fischer 344 rats were administered doses of 0, 300 or 1000 mg/kg/day of Dowfax* C-6 surfactant in deionized water by gavage on days 6 through 15 of gestation. These animals were then allowed to deliver their litters and the litters were evaluated for size, neonatal growth and survival.
Result	:	Administration of oral doses of 300 or 1000 mg/kg/day of Dowfax C-6 surfactant during gestation produced significant depression in maternal weight gain at both dose levels. Evaluation of the litters for mean litter size, neonatal growth and survival through the first 3 days post-partum did not reveal any significant adverse effects at either dose level. Thus, the test material did not appear to have a selective developmental toxicity even at doses producing significant maternal toxicity.
Flag	:	Critical study for SIDS endpoint

24.04.2002 (40)

Type	:	other: OECD 421 reproduction/developmental toxicity study
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	at least 42 days for males and up to 54 days for females
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	14 days
Female	:	14 days
Duration of test	:	
No. of generation studies	:	
Doses	:	60, 200 and 1000 mg/kg/day active ingredient corresponds to 125, 417 and 2083 mg/kg/day Dowfax C6L
Control group	:	yes, concurrent vehicle
NOAEL parental	:	= 200 mg/kg bw
NOAEL F1 offspring	:	= 200 - mg/kg bw
Method	:	OECD Guide-line 421
Year	:	
GLP	:	yes

Test substance : as prescribed by 1.1 - 1.4

Method : Groups of 12 male and 12 female Sprague Dawley rats were administered 0, 60, 200 or 1000 mg/kg/day active ingredient (corresponding to 0, 125, 417 or 2083 mg/kg/day Dowfax C6L respectively). The vehicle, distilled water, was administered at a dose volume of 4 ml/kg. Animals were observed daily for clinical signs. Body weights and feed consumption were obtained during the premating, gestation, lactation and post-mating periods. After two weeks of vehicle or test material administration, the females were cohabitated with males, one male to one female, from the same treatment group, for up to 14 days. Vaginal smears were evaluated daily in females during the 14-day period to establish estrous cyclicity. Once mating was confirmed on gestation day 0 (GD 0), females were separated from the male for the remainder of gestation and allowed to deliver and nurse litters until lactation day (LD) 4. Observations of the F1 pups included survival at birth and during lactation, individual pup body weights and sex, and clinical examinations on LD0 and 4. Complete necropsies were performed on all adult animals. At necropsy, terminal body weights as well as kidney and liver weights were obtained, In addition, testes and epididymides weights were obtained from all males. The following tissues were examined microscopically: kidney, liver and pituitary gland from all animals. In addition, epididymides, prostate, seminal vesicles w/coagulating glands and testes were examined from males and mammary gland, ovaries, oviducts, uterus with cervix and vagina were examined from females. Pups that survived to scheduled euthanasia (LD4) were examined externally and subjected to a complete gross necropsy.

Statistical analysis:
Group Pair-Wise Comparisons - For sample sizes for groups of 3 or greater, Levene's test was used to assess homogeneity of group variances for each specified endpoint and for all collection intervals. If Levene's test was not significant ($p>0.01$), a pooled estimate of the variance was computed from a one-way analysis of variance and utilized by a Dunnett's comparison of each treatment group with the control group. If Levene's test was significant ($p<0.01$), comparisons with the control group were made using Welch's t-test with a Bonferroni correction.
Arcsin-Square-Root Transformation - Data comprised of percent values were transformed using the arcsin of the square root. The analysis described in the Group Pair-wise Comparisons section was then used to analyze the transformed percentage values.
Fisher's Exact Test - An overall test for association between response and treatment was conducted using a Fisher's exact test. If this overall test was significant ($p<0.05$) and there were more than two groups, then a follow up analysis was done, where each treatment group was compared to the control group using a Fisher's exact test.
Covariate Analysis - For the mean of pup body weights per dam and time period, an analysis of covariance using litter size as a covariate was conducted to compare treatment groups. Each treatment was compared to control using Dunnett's test under the analysis of covariance model.

Results were reported at the 0.05 and 0.01 significance levels. All endpoints were analyzed using two-tailed test.

Result : Two males and four females in the high dose group died during the course of the study. The males died on study days 49 and 57 while the females died on premating day 4, GD16, LD1 and LD3. These effects were considered to be test material related.

Decreased activity, salivation, soft and watery feces, audible and difficult breathing were observed in the high dose male rats. Most of the clinical observations were related to the animals that died. During the premating,

gestation and lactation period, similar clinical findings were observed in the high dose female rats but with a lower frequency.

Mean body weights of treated male rats were comparable to control values throughout the study. Mean body weight gain of the high dose male rats was statistically significantly decreased during the first two weeks of premating. A slight decrease was noted at the end of the study in the high dose male rats.

Mean body weights of treated female rats were comparable to control values throughout the study. Body weight changes in females were significantly decreased in the high dose group (1000 mg/kg/day) at GD interval 14-20 (Table 1). The decrease in body weight was considered to be treatment-related. During lactation, body weight changes in low dose female rats was significantly decreased from control values. This was not observed in female rats dosed at 200 or 1000 mg/kg/day. This was considered to not be treatment-related since there was no dose-response relationship and mean body weight values were comparable to control values.

Feed consumption was comparable between male groups. In female rats, feed consumption in the groups administered test material was not significantly decreased in the premating and gestation periods. In the low dose group, female rats had a statistically significant decrease during laction which correlated with the body weight change.

Mean estrous cycle length and number of estrous cycles were comparable among the groups, including control.

There were no treatment-related organ weight changes noted in rats of either sex.

At necropsy, there were no treatment-related gross pathologic observations. One animal that died during the study had discolored liver which corresponded microscopically with minimal focal necrosis. This finding was not noted in any other animal at scheduled necropsy. All other macroscopic and microscopic changes were typical of those commonly observed in rats of the same stain and age and were considered to be incidental.

Reproductive Performance:
There were no test material related changes in mating, fertility and fecundity indices in male and female rats (Table 2). The copulatory interval was increased slightly in the high dose group, but the value (3.8 days) was within the historical control range of 2 to 4.8 days.

Gestation length and gestation index, number of pups born per litter, number of dead pups, stillborn index, and total implantation scars per litter were not affected (Table 3). On LD4, pup sex ratio and mean number of live pups/litter were comparable among the groups. The pup viability index for the high dose animals was slightly decreased at 85.9%, as compared to the control value of 97.2%.

Several pups in the high dose group were observed with decreased activity and cold to the touch. Each observation was observed in ten or less pups on LD0 and only one pup was cold to the touch on day 4. Pup body weight by sex and both sexes combined was significantly reduced in the high dose group on LD0 (Table 4). Similarly, on LD4, male pup body weights and both sexes combined were significantly reduced in the high dose group. However, female pup body weight on LD4 was decreased but not significantly. There were no grossly visible lesions observed in either sex on LD4.

Test substance : Dowfax C6L was determined to contain 50.66% water using Karl Fischer volumetric titration. The purity of the sample was found to be (by difference) 43.4% using ion chromatography and Neutron Activation Analysis. Infrared spectroscopy (FTIR) and liquid chromatographic mass spectroscopy (LC/MS) were used to confirm the proposed structure of Dowfax C6L.

Attached document : Table 1

An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 11 **Summary of Gestation Body Weight Change Values**

Endpoint	Study Interval (Day)	0 mg/kg/day (Vehicle Control) Mean	SD	N	60 mg/kg/day Mean	SD	N	200 mg/kg/day Mean	SD	N	1000 mg/kg/day Mean	SD	N
Body Weight Change Values g													
	0-7	41.2	8.57	12	38.3	6.45	8	35.5	14.00	11	30.7	9.64	9
	7-14	31.7	8.54	12	30.6	6.37	8	29.9	6.63	11	27.8	19.21	9
	14-20	81.3	9.19	12	76.6	16.71	8	80.8	5.02	11	66.5*	19.21	8

Attached document : Table 2

An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 24 **Summary of Reproductive and Fertility Parameters**

Endpoint	0 mg/kg/day (Vehicle Control)	60 mg/kg/day	200 mg/kg/day	1000 mg/kg/day
No. Females on Study	12	12	12	12
No. Females Paired	12	12	12	11
No. Females Mated	12	11	12	11
No. Pregnant	12	11	12	11
Female Mating Index	100.0	91.7	100.0	100.0
Female Fertility Index	100.0	91.7	100.0	100.0
Female Fecundity Index	100.0	100.0	100.0	100.0
No. Males on Study	12	12	12	12
No. Males Paired	12	12	12	11
No. Males Mated	12	11	12	11
No. Males Impregnating a Female	12	11	12	11
Male Mating Index	100.0	91.7	100.0	100.0
Male Fertility Index	100.0	91.7	100.0	100.0
Male Fecundity Index	100.0	100.0	100.0	100.0

No. - Number

Attached document : Table 3

An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 25 **Summary of Natural Delivery and Litter Data**

Endpoint		0 mg/kg/day (Vehicle Control)	60 mg/kg/day	200 mg/kg/day	1000 mg/kg/day
No. Females on Study	N	12	12	12	12
No. Females Pregnant	N	12	11	12	11
Female Fertility Index	%	100.0	91.7	100.0	100.0
Females Delivering Litters[1]	N	12	11	12	10
	%	100.0	100.0	100.0	90.9
With Stillborn Pups[1]	N	2	1	1	1
	%	16.7	9.1	8.3	10.0
With All Stillborn[1]	N	0	0	0	0
	%	0.0	0.0	0.0	0.0
Gestation Length (Days)	Mean	21.9	21.9	22.2	22.0
	SD	0.51	0.35	0.40	0.00
	N	12	8	11	7
No. of Pups at Day 0 (Total Pups Born/Litter)	Mean	15.1	12.0	14.1	14.2
	SD	2.07	4.56	1.31	1.14
	N	12	11	12	10
Live on Day 0/Litter	Mean	14.8	11.9	13.8	12.8
	SD	1.91	4.61	1.76	2.78
	N	12	11	12	10

SD - Standard Deviation
N - Number of measures used to calculate mean
No. - Number
[1]Not statistically analyzed

An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 25 **Summary of Natural Delivery and Litter Data**

Endpoint		0 mg/kg/day (Vehicle Control)	60 mg/kg/day	200 mg/kg/day	1000 mg/kg/day
No. Live Pups/Litter					
Day 4	Mean	14.3	11.8	13.8	13.5
	SD	1.87	4.56	1.76	0.93
	N	12	11	12	8
Sex Ratio (% Males per Animal)					
Pups Day 0	Mean %/Litter	55.54	53.07	52.72	49.76
	SD	14.362	14.768	7.891	14.089
	N	12	11	12	9
Pups Day 4	Mean %/Litter	55.58	53.42	52.96	47.71
	SD	13.914	14.820	7.506	12.883
	N	12	11	12	8
Pup Survival Indices					
Viability Index	Mean %/Litter	97.23	99.39	99.44	85.91
	SD	3.459	2.010	1.925	32.453
	N	12	11	12	9

Attached document : Table 4

An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 27 **Summary of Pup Body Weight Values, g**

Study Interval	Sex		0 mg/kg/day (Vehicle Control)	60 mg/kg/day	200 mg/kg/day	1000 mg/kg/day
Day 0						
	Males	Mean	6.51 (6.56)	6.50 (6.47)	6.70 (6.71)	5.73 (5.71)[b]
		SD	0.470	0.490	0.432	0.732
		N	12	11	12	10
	Females	Mean	6.14 (6.14)	6.21 (6.20)	6.32 (6.33)	5.37 (5.37)[a]
		SD	0.403	0.648	0.403	0.798
		N	12	11	12	10
	Males + Females	Mean	6.34 (6.38)	6.35 (6.31)	6.52 (6.53)	5.55 (5.54)[b]
		SD	0.424	0.549	0.417	0.750
		N	12	11	12	10
Day 4						
	Males	Mean	10.09 (10.34)	10.56 (10.29)	10.25 (10.37)	9.07 (8.90)[b]
		SD	0.939	1.388	0.804	1.054
		N	12	11	12	8
	Females	Mean	9.55 (9.54)	10.05 (9.97)	9.86 (9.86)	8.58 (8.69)
		SD	1.062	1.467	0.813	1.155
		N	12	11	12	8
	Males + Females	Mean	9.87 (10.07)	10.31 (9.91)	10.07 (10.20)	8.82 (8.89)[a]
		SD	0.928	1.420	0.782	1.103
		N	12	11	12	8

SD - Standard Deviation
N - Number of measures used to calculate mean
( ) - Least square mean
[a]Significantly different from control; ($p<0.05$)
[b]Significantly different from control; ($p<0.01$)

MPI Research Study Number 133-058
An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 25 **Summary of Natural Delivery and Litter Data**

Endpoint		0 mg/kg/day (Vehicle Control)	60 mg/kg/day	200 mg/kg/day	1000 mg/kg/day
No. of Pups at Day 0 cont.					
Stillborn	Mean	0.3	0.1	0.3	0.6
	SD	0.45	0.30	0.87	1.90
	N	12	11	12	10
Gestation Index	%	100.0	100.0	100.0	91.0
	N	12	11	12	10
Stillborn Index	Mean %/Litter	1.50	0.91	1.79	4.00
	SD	2.727	3.015	6.188	12.649
	N	12	11	12	10
Total Implantation Scars/Litter	Mean	15.9	14.1	15.3	14.9
	SD	1.93	4.59	1.54	1.10
	N	12	11	12	10

SD - Standard Deviation
N - Number of measures used to calculate mean
No. - Number

MPI Research Study Number 133-058
An Oral Reproduction/Developmental Toxicity Screening Test of DOWFAX C6L in CD Rats

Table 25 **Summary of Natural Delivery and Litter Data**

Endpoint		0 mg/kg/day (Vehicle Control)	60 mg/kg/day	200 mg/kg/day	1000 mg/kg/day
No. Live Pups/Litter					
Day 4	Mean	14.3	11.8	13.7	13.5
	SD	1.67	4.56	1.72	0.93
	N	12	11	12	8
Sex Ratio (% Males per Animal)					
Pups Day 0	Mean %/Litter	55.18	53.07	52.34	49.76
	SD	14.177	14.768	8.139	14.089
	N	12	11	12	9
Pups Day 4	Mean %/Litter	55.58	53.42	52.96	47.71
	SD	13.914	14.820	7.506	12.883
	N	12	11	12	8
Pup Survival Indices					
Viability Index	Mean %/Litter	96.67	99.39	98.59	85.91
	SD	3.508	2.010	3.110	32.453
	N	12	11	12	9

SD - Standard Deviation
N - Number of measures used to calculate mean
No. - Number

Conclusion : Mortality and clinical signs of toxicity were observed in parental animals from the high dose group, 1000 mg/kg/day. Body weight changes were also affected in the high dose group during gestation. In pups, test material related clinical signs and body weight effects were observed in the high dose group and these findings were observed in conjunction with maternal toxicity. Based on the results of this study, the No-Observed-Effect-Level (NOEL) for maternal and developmental toxicity was considered to be 200 mg/kg/day.

Reliability : (1) valid without restriction
1a: GLP guideline study

05.06.2006 (34)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1) Krips, H.J., Determination of the Melting Temperature of Dowfax* Dry Hydrotrope Powder, NOTOX Project 233472, NOTOX Substance 81126, 30 September, 1998, for Dow Chemical Europe, Horgen, Switzerland.

(2) The Dow Chemical Company, 2001, using EPIWIN, Version 2, February 1997 from Syracuse Research Corp.

(3) The Dow Chemical Company, 2001.

(4) Krips, H.J., Determination of the Density of Dowfax* Dry Hydrotrope Powder, HOTOX Project 233483, NOTOX Substance 81126, September 30, 1998, for Dow Europe, SA, Horgen, Switzerland.

(5) Krips, H.J., Determination of the Particle Size Distribution of Dowfax* C6L, NOTOX Project 233538, NOTOX Substance 81126, October 10, 1998, for Dow Europe, SA, Horgen, Switzerland.

(6) Krips, H.J., Determination of the Vapour Pressure of Dowfax* Dry Hydrotrope Powder, NOTOX Project 256567, NOTOX Substance 81126, April 27, 1999, for Dow Europe, SA, Horgen, Switzerland.

(7) Brekelmans, M.J.C., Determination of the Partition Coefficient (n-Octanol/Water) of Dowfax* Dry Hydrotrope Powder, NOTOX Project 233505, NOTOX Substance 81126, September, 29, 1998, for Dow Chemical Europe, SA, Horgen, Switzerland.

(8) Brekelmans, M.J.C., Determination of the Water Solubility of Dowfax* Dry Hydrotrope Powder, NOTOX Project 256556, NOTOX Substance 81126, March 24, 1999, for Dow Chemical Europe, SA, Horgen, Switzerland.

(9) Krips, H.J., Determination of the Surface Tension of an Aqueous Solution of Dowfax* Dry Hydrotrope Powder, NOTOX Project 233494, NOTOX Substance 81126, September 30, 1998, for Dow Europe, SA, Horgen, Switzerland.

(10) Krips, H. J., Determination of the Self-Ignition Temperature of Dowfax* Dry Hydrotrope Powder, NOTOX Project 233527, NOTOX Substance 81126, September 30, 1998, for Dow Europe, SA, Horgen, Switzerland.

(11) Krips, H.J., Determination of the Flammability of Dowfax* Dry Hydrotrope Powder, NOTOX Project 233516, NOTOX Substance 81126, September 30, 1998, for Dow Europe, SA, Horgen, Switzerland.

(12) Brekelelmans, NOTOX, 's-Hertogenbosch, NL, Dowfax* Dry Hydrotrope Powder: Determination of the Hydrolysis as a Function of pH, NOTOX Project 233549, NOTOX Substance 81126, Report DET 2648, 24 September, 1998, for Dow Europe S.A., Horgen, Switzerland, unpublished Dow report.

(13) Willems, Ir.H., NOTOX BV, 's-Hertogenbosch, The Netherlands, Dowfax* Dry Hydrotrope Powder: Soil Adsorption/Desorption Screening Test (OECD106), NOTOX Project: 233551, NOTOX Substance: 81126, Report DET 2649, 25 September, 1998, for Dow Europe S.A., Horgen, Switzerland, unpublished Dow report.

(14) Desmares-Koopmans, M.J.E., NOTOX, NL, Dowfax* Dry Hydrotrope Powder: Assessment of Ready Biodegradability (C)2 Evolution Test), NOTOX Project 233617, NOTOX Substance 81126, Report DET 2636, 19 Auguest, 1998, for Dow Europe S.A., Horgen, Switzerland, unpublished Dow report.

(15) van Ginkel, C.G., Stroo, C.A., Akzo Nobel Central Research, The Netherlands, Dowfax Dry Hydrotrope Powder: Assessment of Primary Biodegradability in the Continuous Activated Sludge Assay, Akzo Task No. 68994, Report DET-2712, 2 June, 1999, unpublished Dow report, for Dow Europe, S.A., Horgen, Switzerland.

(16) Lepailleur, H., IRCHA report 1986: Etude B. 7953.

(17) Gonsior, S.J., Semi-Continuous Activated Sludge Biodegradability Test for Experimental Surfactants XDS 8174.00, XDS 8292.00, and Dowfax 2A1, ES-932, January 8, 1987, unpublished Dow report.

(18) Bogers, M., RCC-NOTOX, The Netherlands, Dowfax* Dry Hydrotrope Powder: 96-Hour Acute Toxicity in the Carp (Cyprinus Carpio), NOTOX Project 233628, NOTOX Substance 81126, Report DET-2650, January 22, 1999, unpublished Dow report, for Dow Europe S.A., Horgen, Switzerland.

(19) Dill, D.C., Murphy, P.G., Richardson, C.H., Evaluation of the Acute Toxicity of C6 Alkylated DPO Disulfonate, Dowfax* C6 Surfactant, to Representative Aquatic Organisms, ES-694, July 16, 1984, unpublished Dow report.

(20) Bogers, M., NOTOX B.V., The Netherlands, Dowfax* Dry Hydrotrope Powder: Acute Toxicity to Daphnia magna, NOTOXx Project 233639, NOTOX Substance 81126, Report DET-2653, 4 November, 1998, unpublished Dow report, for Dow Europe S.A., Horgen, Switzerland.

(21) Bogers, M., NOTOX B.V., The Netherlands, Dowfax* Dry Hydrotrope Powder: Algal Inhibition Test with Selenastrum capricornutum, NOTOX Project 233641, NOTOX Substance 81126, Report DET-2652, 2 November, 1998, unpublished Dow report, for Dow Europe, S.A., Horgen, Switzerland.

(22) Desmares-Koopmans, NOTOX, The Netherlands, Dowfax* Dry Hydrotrope Powder: Activated Sludge Respiration Inhibition Test, NOTOX Project 233652, NOTOX Substance 81126, Report DET 2635, 12 August, 1998, for Dow Europe S.A., Horgen, Switzerland, unpublished Dow report.

(23) Gilbert, K.S., Dowfax C6L: Acute Toxicological Properties, 14 March, 1995, unpublished Dow report.

(24) Carreon, R.E., Sodium Mono and Di Hexyl Diphenyl Oxide Disulfonate: Acute Toxicologic Properties, January 15, 1985, unpublished Dow report.

(25) Pels Rijcken, W.R., NOTOX, B.V., The Netherlands, Dowfax* Dry Hydrotrope Powder: Acute Oral Toxicity (Limit Test) in the Rat, NOTOX Project 233562, NOTOX Substance 81126, Report DET 2642, 10 September, 1998, for Dow Europe S.A., Horgen, Switzerland, unpublished Dow report.

(26) Pels Rijcken, NOTOX B.V., The Netherlands, Dowfax* Dry Hydrotrope Powder: Acute Dermal Toxicity (Limit Test) in the Rat, NOTOX Project 233573, NOTOX Substance 81126, Report DET 2644, 17 September, 1998, for Dow Europe S.A., Horgen, Switzerland, unpublished Dow report.

(27) Pels Rijcken, W.R., NOTOX, B.V., The Netherlands, Primary Skin Irritation/Corrosion Study with Dowfax* Dry Hydrotrope Powder in the Rabbit, NOTOX Project 233584, NOTOX Substance 81126, Report DET 2646 21 September, 1998, for Dow Europe S.A., Horgen, Switzerland, unpublished Dow report.

(28) Brooks, K.J., Dowfax* C6L Surfactant (5% Aqueous Solution): Acute Primary Eye Irritation Study in New Zealand White Rabbits, 02 February, 1998, unpublished Dow report, 971198.

(29) Pels Rijcken, W.R., NOTOX, B.V., The Netherlands, Acute Eye Irritation/Corrosion Study with Dowfax* Dry Hydrotrope Powder in the Rabbit, NOTOX Project 233595, NOTOX Substance 81126, Report DET 2645, 18 September, 1998, for Dow Europe S.A., Horgen, Switzerland, unpublished Dow report.

(30) Pels Rijcken, W.R., NOTOX, B.V., The Netherlands, Assessment of Contact Hypersensitivity to Dowfax* Dry Hydrotrope Powder in the Albino Guinea Pig, NOTOX Project 233606, NOTOX Substance 81126, Report DET 2647, 22 September, 1998, for Dow Europe S.A., Horgen, Switzerland, unpublished Dow report.

(31) Cummins, H.A., Ashby, R., Fowler, J.S.L., Dowfax* XD 8292: Four Week Toxicity Study by Oral Administration to CD Rats, DET 975, November 25, 1987, unpublished Dow report.

(32) Hanley, T.R., Jr., Yano, B.L., Dowfax* C-6 Surfactant: 10-Day Repeated oral Gavage Study in Female Fischer 344 Rats, Nov. 21, 1985, unpublished Dow report.

(33) Faqi, A.S. and Makovec, G.T. (2005). A two-week range-finding oral toxicity study of Dowfax C6L in rats. Unpublished report of The Dow Chemical Company.

(34) Faqi, A.S. and Nelson, D.T. (2006). An oral reproduction/developmental toxicity screening test of Dowfax C6L in CD rats. Unpublished report of The Dow Chemical Company.

(35) Lawlor, T.E., Mutagenicity Test on Dowfax* C6L Surfactant in the Salmonella-Escherichia coli/Mammalian-Microsome Reverse Mutation Assay, July 8, 1996, unpublished Dow report.

(36) Verspeek-Rip, C.M., NOTOX B.V., The Netherlands, Dowfax* Dry Hydrotrope Powder: Reverse Mutation Assay in Salmonella typhimurium and Escherichia coli (with independent repeat), NOTOX Project 244698, NOTOX Substance 81126, Report DET-2674, 14 January, 1999, unpublished Dow report, for Dow Europe, S.A., Horgen, Switzerland.

(37) Enninga, I.C., Dowfax* XD 8292: Chromosomal Aberration Assay with Cultured Peripheral Human Lymphocytes in vitro, November 25, 1987, DET 974, unpublished Dow report(s).

(38) Linscombe, V.A., Shabrang, S.N., Evaluation of Dowfax* C6L Surfactant in an in vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes, August 7, 1996, unpublished Dow report.

(39) Linscombe, V.A., Day, S.J., Evaluation of Dowfax* Dry Hydrotrope Powder in an in vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes, 15 December, 1998, unpublished Dow report.

(40) Hanley, T.R. Jr., Berdasco, N.M., Yano, B.L., Dowfax* C-6 Surfactant: Chernoff Test in Female Fischer 344 Rats, 11 June, 1985, unpublished Dow report.

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT

IUCLID

Data Set

Existing Chemical	:	ID: 65143-89-7
CAS No.	:	65143-89-7
Producer Related Part		
Company	:	The Dow Chemical Company
Creation date	:	23.08.2001
Substance Related Part		
Company	:	The Dow Chemical Company
Creation date	:	23.08.2001
Memo	:	
Printing date	:	15.12.2003
Revision date	:	
Date of last Update	:	15.08.2002
Number of Pages	:	79
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	???

1.0.1 OECD AND COMPANY INFORMATION

Type : lead organisation
Name :
Partner :
Date :
Street :
Town :
Country :
Phone :
Telefax :
Telex :
Cedex :
23.08.2001

Type : lead organisation
Name :
Partner :
Date :
Street :
Town :
Country :
Phone :
Telefax :
Telex :
Cedex :
23.08.2001

1.0.2 LOCATION OF PRODUCTION SITE

Name of Plant : Pilot Chemical
Street : 606 Shepherd Drive
Town : 45215 Lockland, Ohio
Country : United States
Phone :
Telefax :
Telex :
Cedex :
21.01.2002

Name of Plant : Pilot Chemical
Street : 3439 Yankee Road
Town : 45042 Middletown, Ohio
Country : United States
Phone :
Telefax :
Telex :
Cedex :
21.01.2002

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

Substance type : organic
Physical status : solid
Purity : % w/w
Remark : This CAS RN (65143-89-7) represents the monoalkylated/disulfonated/disodium salt. The commercial product is made up of both CAS RN 65143-89-7 and CAS RN 70191-76-3 (dialkylated/disulfonated/disodium salt) with more of the product being the former. The US product MSDS states that 15-35% is CAS 65143-89-7 and 5-10% is CAS 70191-76-3.

NOTE: See letters on file with EPA and the Test Plan for HPV for further explanation of CAS RN usage.

The commercial product is normally about 50% solids in water. Use concentrations may be less. Some toxicity (irritancy) data have been generated on the use concentrations. Most of the tox information is for the 50% aqueous solution and some is for the dry solid.

08.04.2002

Substance type : organic
Physical status : solid
Purity : % w/w
Remark : This CAS RN (96024-29-2) represents the commercial mixture. The commercial product is made up of both CAS RN 65143-89-7 and CAS RN 70191-76-3 (dialkylated/disulfonated/disodium salt) with more of the product being the former. The US product MSDS states that 15-35% is CAS 65143-89-7 and 5-10% is CAS 70191-76-3.

The commercial product is normally about 50% solids in water. Use concentrations may be less. Some toxicity (irritancy) data have been generated on the use concentrations. Most of the tox information is for the 50% aqueous solution and some is for the dry solid.

06.12.2001

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

Benzenesulfonic acid, hexadecyl(sulfophenoxy)-, disodium salt
23.08.2001

Benzenesulfonic acid, oxybis[hexadecyl-, disodium salt (CAS RN 70191-76-3)
23.08.2001

Disodium dihexadecyldiphenyloxide disulfonate (CAS RN 70191-76-3)
23.08.2001

Disodium hexadecyldiphenyloxide disulfonate
23.08.2001

Dowfax Detergent
22.03.2002

Dowfax* 8390 Solution Surfactant
23.08.2001

Dowfax* 8390-D Surfactant (solid)
23.08.2001

Hexadecyl(sulfophenoxy)benzenesulfonic acid, disodium salt
23.08.2001

Oxybis(hexadecylbenzenesulfonic acid), disodium salt (CAS RN 70191-76-3)
23.08.2001

XDS-8390
23.08.2001

XU-040341.00
24.08.2001

1.3 IMPURITIES

CAS-No : 7757-82-6
EINECS-No : 231-820-9
EINECS-Name : sodium sulphate
Contents : <= 1.5 % w/w
23.08.2001

CAS-No : 7647-14-5
EINECS-No : 231-598-3
EINECS-Name : sodium chloride
Contents : < 1 % w/w
Remark : Amounts shown are for the aqueous commercial solution.
23.08.2001

1.4 ADDITIVES

1.5 QUANTITY

Production during the last 12 months :
Import during the last 12 months :
Quantity : 100 - 500 tonnes in 1999
Remark : Sold globally
04.06.2002

1.6.1 LABELLING

Labelling : provisionally by manufacturer/importer
Symbols : XiN
Nota :
Specific limits :
R-Phrases : (36) Irritating to eyes
(41) Risk of serious damage to eyes
(50/53) Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S-Phrases : (25) Avoid contact with eyes
(26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice

(61) Avoid release to the environment. Refer to special instructions/Safety data sets

Remark : Labeling is for the aqueous commercial solution.
23.08.2001

1.6.2 CLASSIFICATION

Classification : provisionally by manufacturer/importer
Class of danger : dangerous for the environment
R-Phrases : (50/53) Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

23.08.2001

Classification : provisionally by manufacturer/importer
Class of danger : irritating
R-Phrases : (36) Irritating to eyes
(41) Risk of serious damage to eyes
Remark : Classifications are for the aqueous commercial solution.
23.08.2001

1.7 USE PATTERN

Type : type
Category : Wide dispersive use
11.12.2001

Type : industrial
Category : Chemical industry: used in synthesis
11.12.2001

Type : industrial
Category : Paints, lacquers and varnishes industry
11.12.2001

Type : industrial
Category : Textile processing industry
11.12.2001

Type : industrial
Category : other
11.12.2001

Type : use
Category : Cleaning/washing agents and disinfectants
11.12.2001

Type : use
Category : Surface-active agents
11.12.2001

1.7.1 TECHNOLOGY PRODUCTION/USE

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.9 SOURCE OF EXPOSURE

Memo : Addition
Remark : Exposure is estimated using the EASE model. Inhalation exposure during addition is assumed to concern non-dispersive use in the presence of LEV. Partial vapor pressure was calculated to be 0.9 Pa, assuming an ideal mixture. This leads to a predicted negligible exposure level. Dermal exposure is also possible during addition of the substance. The predicted dermal exposure to the substance is assessed by expert judgment to be 10-40% of the cleaning activities (with 1% solution), correcting for the percentage of substance in the solution. Exposure during cleaning of the working area or maintenance to the equipment is also possible, but is considered to be less than exposure assessed in this scenario.

10.06.2002

Memo : Cleaning
Remark : Exposure during professional cleaning may occur when using products that contain up to 1% of the substance. Inhalation exposure is estimated with EASE, assuming wide-dispersive use, direct handling and no dilution ventilation. The predicted level of exposure is negligible, using a partial vapor pressure of 0.01*2.67 Pa. Dermal exposure during these activities is, however, possible. Using EASE, dermal exposure is predicted to be 5-15 mg/cm2/day, assuming wide-dispersive use, direct handling and an extensive contact level. When assuming an exposed area of 1300 cm2 (approx. the surface area of both hands and a part of the forearms) assessed duermal exposure is 195 mg/day (15 x 1300 x 0.01).

There is no information about the number of workers exposed, the frequency and duration of exposure for the scenarios mentioned overall. The number of workers and frequency of use have been estimaed to be:

	# of workers	frequency (da/yr)
-addition	30-50	220
-filling	<20	220
-cleaning	<200	220

10.06.2002

Memo : Consumers
Remark : Consumers will be potentially exposed by contact with plastic articles prepared with the aid of the substance, by wearing clothes prepared with the aid of the substance, and by using cleaning agents/disinfectants containing the substance (hospitals). The main route of potential exposure is through the skin. The exposures to these sources are considered to occur simultaneously as a worst case.

1. Consumer exposure by the use of disinfectants in hospitals is estimated with the EUSES scenario for 'substances contained in a medium', using a subchronic timescale, a contact time of one hour and an exposure frequency fo 10 events/day. The concentration of the substance in the end products (i.e., before dilution) is max. 1% and 10g of the product is assumed to be used on each event.

Uptake by the use of disinfectants is thus estimated to be 0.0326 gm/kg/day.

2. Consumer exposure by contact with plastic articles is estimated with the EUSES scenario for 'substances migrating from an article', using a subchronic timescale, a contact time of 8 hrs (per day) and an exposure frequency of 1 event/day. The concentration fo the substance in the plastics is estimated to amount to 1%. The fraction migrating per day is assumed to be 0.001.

The uptake by contact with plastics is thus estimated to be 4e-04 mg/kg/day.

3. Consumer exposure by wearing clothing is estimated with the EUSES scenario for 'substances contained in amedium', using a subchronic timescale, a contact time of 16 hrs/day and an exposure frequency of 1 event/day. The concentration of the substance in the clothing is estimated to amount to 1%. The fraction migrating per day is assumed to be 0.001.

The uptake by contact with clothing is thus estimated to be 0.0185 mg/kg/day.

Total:

The total daily uptake is estimated to be 0.0515 mg/kg/day resulting in a margin of safety of 4854 (=250/0.0515).

10.06.2002

Memo : Filling
Remark : During filling of cartridges inhalation exposure is assessed to be negliible, assuming non-dispersive use in the presence of LEV and a partial vapor pressure of <1Pa. Dermal exposure is assessed to be 0-1% (concentration and dose) of scenario 3 (expert judgment), correcting for the amount of substance in ink. Exposure during cleaning of the working area or during maintenance of the equipment is also possible, but is considered to be smaller than the exposure assessed for the filling scenario.

10.06.2002

Memo : Indirect Exposure via the Environment
Remark : The total daily intake via air, drinking water and food is estimated to be 1.58e-03 -- 0.162 mg/kg/day at the local scale (depending on the branch of industry) and 2.6e-04 mg/kg/day at the regional scale.

10.06.2002

Memo : Occupational Exposure
Remark : The substance is an off-white powder that is marketed as a 35% solution (mixture) in water (non-viscous aqueous yellow to amber solution). The substance is/will be used (in Europe) as either process regulator or surface active agent in the chemical industry (35% as chemical used in process industry and 30% in base chemistry), the textile industry (20%, and for personal/domestic purposes (cleaning agents 15%).

Two special application of the substance are:
-Monet type ink used in ink jet printers for office and personal use
-Preparation (35%) with use in textile industry

In most applications the subnstance is used in diluted form. For cleaning agents the concentrations used are less than 1%. The content of the substance in the ink is 0.13%. For the other purposes it is assumed that 35% solutions are used.

Exposure to the substance used in 35% solution is possible in the textile industry and chemical industry in the following situations:
-adding the substance to the blender or a process;
-blending;
-application;
-cleaning and maintenance;
-quality control sampling.

Exposure to Monet type ink (0.13% solution) can take place during filling of the ink cartridges and cleaning and maintenance activities of the area

where the cartridges are filled with ink. Use of the cartridges (e.g. changing cartridges) by users may also lead to exposure to the substance, but is not considered to be relevant because of the low percentage of the substance in the cartridge and the probably low frequency and duration of consumer exposure.

Dermal exposure to the substance is possible during mixing and leading products containing </= 1% of the substance for cleaning and during the cleaning itself.

Exposure to the eyes may occur due to splashing with a solution or due to hand-eye contact.

The following exposure scenarios are considered to be relevant:
-addition of the substance (35% solution) to the process or bender (addition);
-filling cartridges with ink (filling);
-cleaning activities with </= 1% solution (cleaning).

For these scenarios potential exposures were assessed. Exposure reducing PPE was not considered in the assessment.

10.06.2002

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

Type : Handling
Remark : Avoid eye contact. Avoid breathing mists. Avoid trapping material under clothing.

Good general ventilation should be sufficient for most conditions. Local exhaust ventilation may be necessary for some operations.

For most conditions, no respiratory protection should be needed; however, in misty atmospheres, use an approved mist respirator.

When prolonged or frequently repeated contact could occur, use protective clothing impervious to this material. Selection of specific items such as face shield, gloves, boots, apron, or full body-suit will depend on operation.

Use chemical goggles.

23.08.2001

Type : Storage
Remark : Stable under normal handling and storage conditions.

No hazardous decomposition products under normal conditions of storage and use. Sulfur and carbon oxidation products.

Storage areas to be equipped with spill collection system.

23.08.2001

Type : Fire
Remark : This material will not burn until water has evaporated.
23.08.2001

1.10.2 EMERGENCY MEASURES

Type : accidental spillage

Remark : Wear adequate personal protective equipment.

Contain liquid to prevent contamination of soil, surface water or ground water.

Small spills: Cover and soak up with a suitable absorbent material.
Large spills: Contain with dike. Pump into suitable and properly labelled containers.
Residues: Cover and soak up with a suitable absorbent material. Clean area with water.

23.08.2001

Type : injury to persons (skin)
Remark : Wash off in flowing water or shower.
If burn is present, treat as any thermal burn, after decontamination.

23.08.2001

Type : injury to persons (eye)
Remark : Irrigate with flowing water immediately and continuously for 15 minutes.
Consult medical personnel.

23.08.2001

Type : injury to persons (oral)
Remark : Never give fluids or induce vomiting if patient is unconscious or is having convulsions.
If swallowed, seek medical attention. Do not induce vomiting unless directed to do so by medical personnel.
Supportive care. Treatment based on judgment of the physician in response to reactions of the patient.
No specific antidote.

23.08.2001

Type : injury to persons (inhalation)
Remark : Remove to fresh air if effects occur. Consult a physician.
23.08.2001

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

Memo : Incinerate under controlled conditions in accordance with all local and national laws and regulations.

23.08.2001

Memo : Empty containers can only be disposed of when the remaining waste products adhering to the container walls have been removed. hazard warning labels should be removed from the container walls.

23.08.2001

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

Memo : Consumer Risk
Remark : The margin of safety between the dermal NOAEL-rat (uptake basis, derived from the oral NOAEL, assuming the bioavailability for both the oral and dermal route is 100%) and the estimated total daily uptake has been calculated to be 4854. Taking into account all data available, this margin of safety is judged to be sufficient.

10.06.2002

Memo : Man Exposed Indirctly via the Environment
Remark : The margin of safety between the 28-day NOAEL-rat and the highest estimated total daily intake has been calculated to be 1.54e+03 -- 1.58e+05. Taking into account all data available, this margin of safety is judged to be sufficient. It is concluded that the substance is not expected to pose a risk to the public at large at the local scale.

10.06.2002

Memo : Risk Estimation
Remark : From the oral 28-day subchronic toxicity study a NOAEL of 250 mg/kg for the substance is established. This level is used to estimate the risk for adverse systemic health effects. Extrapolation to humans (assuming 50% absorption from the gastrointestinal tract, 70 kg body weight, an extrapolation- and uncertainty factor of 1000) results in an internal Health Based Occupational Reference Value for the worker (HBORV-intern) of 8.7 mg/day. Assuming 100% retention in the respiratory tract (worst case), an HBORV-inh of 8.7 mg/day is derived. Given the molecular weight and the octanol/water partition coefficient, absorption through the skin cannot be excluded. For the risk estimation 10% absorption is taken as worst case, resulting in an HBORV-derm of 87 mg/day.

Occuptional Scenario	Est. Exposure dermal (mg/day)	Est. Exposure inhal (mg/day)	Exceeding Factor derm.	Exceeding Factor inh.
addition	19.5	negl.	<1	<1
filling	2	negl.	<1	<1
cleaning	195	negl.	2.2	<1

Comparison of the HBORVs with exposure estimates leads to the conclusion that, for dermal exposure in 'cleaning', the substance is of concern for workers with respect to adverse systemic health effects after repeated dermal exposure. This risk characterization is made with a number of worst case assumptions and can be refined with data on e.g., actual exposure, dermal/respiratory absorption, and data on dermal and respiratory repeated-dose toxicity. In view of the exceeding factor as determined in the above risk calculation, risk reduction measures are required. It should be noted that the risk for local effects after repeated dermal exposure and inhalation exposure can only be estimated with results from toxicity studies performed with the respective exposure routes.

10.06.2002

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

Type : TSCA
Additional info :
23.08.2001

Type : AICS
Additional info :
23.08.2001

Type : NDSL
Additional info :
23.08.2001

Type : PICCS
Additional info :
23.08.2001

Type : TSCA
Additional info :
Remark : Found for CAS 65143-89-7 and for 70191-76-3.
06.12.2001

Type : AICS
Additional info :
Remark : Found for CAS 65143-89-7 and for 70191-76-3.
06.12.2001

Type : NDSL
Additional info :
Remark : Found for CAS 65143-89-7
06.12.2001

Type : PICCS
Additional info :
Remark : Found for CAS 65143-89-7
06.12.2001

Type : DSL
Additional info :
Remark : Found for CAS 70191-76-3.
06.12.2001

2.1 MELTING POINT

Decomposition	:	yes at ca. 230 ° C
Sublimation	:	
Method	:	other: both OECD 102 and EEC 84/449
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The capillary method was used. Approx 109 g. of the test substance was dried for 10 hrs in a rotary evaporator, then in a stove for 4 days at 60C. This produced a yellow-brown powder which was ground. The weight of ground powder was 40.6g. This substance was put on a petri dis and deried in a stove for another 22 hrs at a temp of approx. 60C. The remaining off-white powder was used for the melting point determination. The measurement was carried out using a Buechi 512, containing a liquid bath melting point device. A small amount of the substance was charged in a capillary glass tube and packed tightly. The tube was heated together with a thermometer and the temperature rise was adjusted to 3.0 K/min. Changes in consistence of the test subswtance and corresponding temperatures were registered.
Result	:	A fast rough determination showed consistency changes but no melting below 310C. So the test was repeated in duplicate. Observations were started at 220C with an adjusted temp rise of 3.0 C per minute. The test substance began producing air bubbles at about 230C and continued to turn 'foamy' up to 250C. Discoloration of the test material also took place--changing from off-white to red-brown. Thus, the melting point/range of Dowfax 8390 could not be determined. The test substance started to disintegrate at approx 230C before reaching a melting point.
Test substance	:	Dowfax 8390 conmtaining 36.7% active ingredient, but which was evaporated to dryness prior to the test.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (1)

Value	:	= 320 ° C
Sublimation	:	
Method	:	other
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Melting Point, Boiling Point, and Vapor Pressure were estimated using Estimation Programs Interface (EPIWIN, Version 2, February, 1997) available from Syracuse Research Corporation (Syracuse, NY). Estimations of properties for representative isomers are based on quantitative structure-activity relationships.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

30.10.2001 (2)

2.2 BOILING POINT

Value	:	= 99.6 - 100.1 ° C at 101.325 hPa

Decomposition	:	
Method	:	other: both EEC 84/449 and OECD 103
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The capillary tube method was used. The measurement was carried out using a Buechi 512 containing a liquid bath melting point device. A capillary glass tube was filled with the test substance to a height of 5-10 mm. The determinations were started at a temperature of approx 92C. At this temp. Dowfax 8390 was in a liquid phase. A boiling capillary was immersed int he test substance, whereafter the capillary glass tube was heated together with a thermometer and the temperature ruse was adjusted to 0.5 K/min. A quick, rough estimate was made and that was followed by a triplicate determination. Measurements started at approx. 92C. At this temperature the test substance was a light red-brown liquid and air bubbles already started to appear. With increasing the temperature, the amount of air bubbles increased and no change in color or viscosity was observed. The stream of air bubbles reached a maximum at 99.6-100.1C. When increasing the temperature to 190C the test substance changed into a white solid substance. All measurements were performed at atmospheric pressure.
Remark	:	Assumed hPa and kPa are the same (pressure reading at boiling point). The test substance was not evaporated prior to the test. It is likely that the boiling observed was the water boiling off (about 100C). The test substance was only heated to about 190C in this test, driving off the water, but not high enough to decompose it. This is as anticipated.
Test substance	:	The test sample was Dowfax 8390 containing 36.7% active ingredient in water.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (3)

Value	:	= 730 ° C at
Decomposition	:	
Method	:	other
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Melting Point, Boiling Point, and Vapor Pressure were estimated using Estimation Programs Interface (EPIWIN, Version 2, February, 1997) available from Syracuse Research Corporation (Syracuse, NY). Estimations of properties for representative isomers are based on quantitative structure-activity relationships.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

30.10.2001 (2)

2.3 DENSITY

Type	:	density
Value	:	= 1.1011 g/cm3 at 21.3° C
Method	:	Directive 84/449/EEC, A.3 "Relative Density"
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method	:	A pycnometer of 1 ml was used to determine the density of Dowfax 8390. An analytical balance, Mettler type AE 100, with an accuracy of 0.1 mg was used for the weighings. All equipment and materials were at stable room temperatures for the test. The experiment was carried out in the traditional way--in duplicate. The density was determined to be 1.1011 g/cm3 at 21.3C. Individual values fall within the 0.001 g/ml range and therefore meet the quality criteria established pre-test.
Test substance	:	The test substance was Dowfax 8390, containing 36.7% active ingredient in water. The substance was tested 'as is'.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (4)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	< 0 hPa at 25° C
Decomposition	:	
Method		other (calculated)
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Melting Point, Boiling Point, and Vapor Pressure were estimated using Estimation Programs Interface (EPIWIN, Version 2, February, 1997) available from Syracuse Research Corporation (Syracuse, NY). Estimations of properties for representative isomers are based on quantitative structure-activity relationships.
Remark	:	The actual value calculated by SAR was 1.07x10-21 hPa. However, IUCLID may not be able to display that number.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

17.06.2002 (2)

2.5 PARTITION COEFFICIENT

Log pow	:	= 5.9 at 25° C
Method		other (calculated)
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Partition coefficient in environmental pH range of 5 to 9 was estimated using ACD/Log D program (Version 4.56, April 2000) available from ACD Labs (Toronto, Canada). Estimations of Log P for representative isomers were based on quantitative structure-activity relationships which account for dissociation as a function of pH.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

30.10.2001 (2)

2.6.1 WATER SOLUBILITY

Value	:	ca. 100000 mg/l at 25 ° C

Qualitative	:	of very high solubility
Pka	:	at 25 ° C
PH	:	at and ° C
Method	:	other
Year	:	2001
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Water solubility in the environmenatl pH range of 5 to 9 was estimated based on the product formelation information. Formulations contain 10 to 50% of surfactant in water. Thus, solubility is >100,000 mg/L.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

30.10.2001 (2)

2.6.2 SURFACE TENSION

Test type	:	OECD harmonized ring method
Value	:	= 35.5 mN/m at 25 ° C
Concentration	:	36.7 vol%
Method	:	Directive 84/449/EEC, A.5
Year	:	1988
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The procedure used followed that given in Vol. 27 of the Official J. of the European Communities dated 19.9.84 No. L 251 pages 37 to 43, entitled Part A: Methods for the determination of physico-chemical properties, A.f. Surface Tension. All measurements were made at 25C on freshly diluted samples (less than one day old) of Dowfax 8390. The method used follows the OECD harmonized ring tensiometer method. Calibration of the equipment Kruess tensiometer Model K10) was carried out with Laboratory deionized water. Readings were repeated until equilibrium values were obtained in a sequence of 5 minute intervals. The measurements were performed by A. Schmitz on 30th September 1988, at the Dow Rheinmuenster Research Laboratory.
Result	:	Dowfax 8390 Surface Tension m N/m --- (36.7% active) 35.5 100 g/liter 38.6 10 g/liter 40.6 1 g/liter 41.9 0.1 g/liter 45.9 0.01 g/liter 51.7
Test substance	:	The commercially available Dowfax 8390 containing 36.7% active ingredient was used in the test. Further dilutions were made using deionized tap water of conductivity less than 1.24 microS/cm.
Flag	:	Critical study for SIDS endpoint

26.04.2002 (5)

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= 5.4 hour(s)
Degradation	:	% after
Quantum yield	:	
Deg. product	:	
Method	:	other (calculated): AOP v 1.91
Year	:	2006
GLP	:	
Test substance	:	
Result	:	SMILES: c1(Oc2c(C(C)CCCCCCCCCCCCCC)cc(S(O)(O)O)cc2)ccc(S(O)(O)O)cc1 Mol Formula: C28 H46 O7 S2 Mol Wt: 558.79 SUMMARY (AOP v1.91): HYDROXYL RADICALS Hydrogen Abstraction = 20.8262 E-12 cm3/molecule-sec Reaction with N, S and -OH = 0.8400 E-12 cm3/molecule-sec Addition to aromatic rings = 2.3179 E-12 cm3/molecule-sec Overall OH Rate Constant = 23.9840 E-12 cm3/molecule-sec Half life = 0.446 Days (12-hour day, 1.5E6 OH/cm3) Half life = 5.352 Hours 2f: Accepted calculation method

25.07.2006

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at degree C
t1/2 pH7	:	at degree C
t1/2 pH9	:	at degree C
Deg. Product	:	
Method	:	OECD Guide-line 111 "Hydrolysis as a Function of pH"
Year	:	1995
GLP	:	yes
Test substance	:	other TS: solid powder XD-8390
Method	:	This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland. An accurately weighed amount of the test material (range 222-251 mg) was added to 50.0 mlbuffer solution (pH 4.0, 7.0 and 9.0). The filter-sterilized solutions were treated for 5 minutes with nitrogen gas to exclude oxygen. The incubation took place at 50 +/- 0.5C in the dark. The concentration of the test substance was determined by HPLC after 0, 2.4 hours and 5 days. pH values were checked at the beginning and at the end of the test.
Result	:	Dowfax 8390-D surfactant showed no decrease in concentration for any of its components after incubation at 50C at pH 4.0, 7.0 and 9.0 for up to 5 days. Correspondingly, the material can be termed to be hydrolytically stable.
Reliability	:	(1) valid without restriction

Flag : Critical study for SIDS endpoint
26.04.2002 (6)

3.1.3 STABILITY IN SOIL

01.11.2001

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level I
Media :
Air : .1 % (Fugacity Model Level I)
Water : .1 % (Fugacity Model Level I)
Soil : 97.6 % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :

Attached document : Remarks: Level I model version 2.11. Obtained from the Canadian Environmental Modeling Centre, Trent University, Peterborough, Ontario, Canada

Input Parameters for Level I Model:

Property	Value	Source
Data Temperature (°C)	25	
Chemical Type	1	Type 1 indicates chemical can partition into all environmental compartments
Molecular Mass (g/mol)	599	Calculated from molecular structure
Water Solubility (g/m^3)	100,000	Estimated value based on formulation composition [2]
Vapor Pressure @ 25°C (Pa)	1×10^{-12}	Estimated value [3]
Melting Point (°C)	320	Estimated value [3]
Log K_{ow} Octanol-Water Partition Coefficient	5.9	Estimated value [4]
Amount of Chemical input (kg)	100,000	Level I Default Value [1]

RESULTS

Fugacity Level I: Distribution among air, water, soil, and sediments

Emission Scenario	Percentage and amount distributed to			
	Air	Water	Soil	Sediment
100,000 kg total emissions	<0.1 % <1 kg	0.1 % 139 kg	97.6 % 97619 kg	2.2 % 2169 kg

CONCLUSIONS
The environmental distribution and transport of DOWFAX 8390 Surfactant (C18 linear alkyl diphenyl oxide disulfonate, sodium salt) between environmental compartments (air, water, soil, and sediments) was predicted using Level I fugacity model. Input values required for the Level I model include molecular weight, melting point, water solubility, vapor pressure, and octanol/water partition coefficient. The Level I model estimates the Henry's Law constant for the compound, and predicts the distribution of the compound between the environmental compartments assuming that equilibrium is attained.

DOWFAX 8390 Surfactant has little potential to volatilize from aqueous solution, based on the very low estimated Henry's Law constant (6×10^{-15} Pa m^3/mol). The compound has a high potential to bioaccumulate in aquatic organisms based on the estimated log K_{ow} value (5.9). Major applications for the alkyl diphenyl oxide disulfonate surfactants include emulsion polymerization and institutional and industrial cleaning. Based on the physical and chemical properties and known uses of DOWFAX 8390 Surfactant, the compound will be released primarily into water.

Distribution of surface active agents (i.e. surfactants) is governed by interfacial distributions and not by equilibrium partitioning. Thus, the output of the Level 1 fugacity model for DOWFAX 8390 Surfactant is speculative, at best. Also, note that DOWFAX 8390 Surfactant will be ionized in solution due to the low pKa of the sulfonate groups (estimated pK_a <2 [4]). Therefore, partitioning from water to air (i.e. volatilization) or from water to organic phases (i.e. octanol/water partition coefficient) may be significantly less than that predicted for the neutral (uncharged) molecule.

REFERENCES

1. Mackay, D. (2001). Multimedia Environmental Models: The Fugacity Approach. Lewis Publishers, CRC Press, Boca Raton, Florida. Models available at: http://www.trentu.ca/cemc/models.html
2. IUCLID Data Set for DOWFAX 8390 Surfactant. December 17, 2002.
3. U.S. EPA. 2000. EPIWIN software, version 3.11. United States Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D. C. Available at: http://www.epa.gov/oppt/exposure/docs/episuitedl.htm
4. Advanced Chemistry Development, Inc., Toronto, Canada. 2000. ACD/Log D. Version 4.56.

Reliability : (2) valid with restrictions
2f: Accepted calculation method

13.06.2006

Type : fugacity model level III
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :

Attached document : Remarks: Level III model version 2.70. Obtained from the Canadian Environmental Modeling Centre, Trent University, Peterborough, Ontario, Canada

Input Parameters for Level III Model:

Property	Value	Source
Data Temperature (°C)	25	
Chemical Type	1	Type 1 indicates chemical can partition into all environmental compartments
Molecular Mass (g/mol)	599	Calculated from molecular structure
Water Solubility (g/m^3)	100,000	Estimated value based on formulation composition [2]
Vapor Pressure @ 25°C (Pa)	1×10^{-12}	Estimated value [3]
Melting Point (°C)	320	Estimated value [3]
Estimated Henry's Law Constant (H) ($Pa\ m^3/mol$)	6.0×10^{-15}	Calculated by Level I Fugacity Model [1]
Log K_{ow} Octanol-Water Partition Coefficient	5.9	Estimated value [4]
Amount of Chemical input (kg/hr)	1,000 per compartment	Level III Default Values [1]
Reaction Half-lives (hr) Input to Level III Model		
Air (vapor phase)	*11	Estimated value [3]
Water (no susp. solids)	3600	Estimated value [5]
Soil	96	Measured value [6]
Sediment	168	Measured value [7]
Suspended Sediment	$**1.0 \times 10^{11}$	
Fish	$**1.0 \times 10^{11}$	
Aerosol	$**1.0 \times 10^{11}$	

**Default value used in Level III model when reaction is expected to be negligible in this compartment

RESULTS

Fugacity Level III: Distribution among air, water, soil, and sediments

Emission Scenario	Percentage and amount distributed to				Residence Time (days) [without advection in brackets]
	Air	Water	Soil	Sediment	
1,000 kg/hr to Air	<0.1 % <1 kg	8.7 % 13323 kg	86.9 % 1.33×10^5 kg	4.4 % 6746 kg	6 [6]
1,000 kg/hr to Water	**<0.1 % <1 kg**	**66.4 % 3.12×10^5 kg**	**<0.1 % <1 kg**	**33.6 % 1.58×10^5 kg**	**20 [29]**
1,000 kg/hr to Soil	<0.1 % <1 kg	<0.1 % 11 kg	100.0 % 1.39×10^5 kg	<0.1 % 6 kg	6 [6]
1,000 kg/hr simultaneously to Air, Water, and Soil	<0.1 % <1 kg	42.7 % 3.25×10^5 kg	35.6 % 2.71×10^5 kg	21.6 % 1.65×10^5 kg	11 [12]

Highlighted scenario indicates most likely emission distribution, based on use patterns

CONCLUSIONS

The environmental distribution and transport of DOWFAX 8390 Surfactant (C18 linear alkyl diphenyl oxide disulfonate, sodium salt) between environmental compartments (air, water, soil, and sediments) was predicted using a Level III fugacity model. The Level III model requires input of measured or estimated half-lives for reaction in air, water, soil, and sediments along with input values required for the Level I model including molecular weight, melting point, water solubility, vapor pressure, and octanol/water partition coefficient. The Level III model incorporates transport rates into and between environmental compartments, and allows for losses of the compound due to advection or degradation processes.

DOWFAX 8390 Surfactant has little potential to volatilize from aqueous solution, based on the very low estimated Henry's Law constant (6 x 10-15 Pa m3/mol). The compound has a high potential to bioaccumulate in aquatic organisms based on the estimated log Kow value (5.9). Major applications for the alkyl diphenyl oxide disulfonate surfactants include emulsion polymerization and institutional and industrial cleaning. Based on the physical and chemical properties and known uses of DOWFAX 8390 Surfactant, the compound will be released primarily into water. Assuming release into water only, the Level III fugacity model predicts that the compound will be distributed between the water and sediment compartments with a residence time of approximately 20 days. Biodegradation is the major degradation process that affects the predicted residence time for the compound.

Distribution of surface active agents (i.e. surfactants) is governed by interfacial distributions and not by equilibrium partitioning. Thus, the output of the Level III fugacity models for DOWFAX 8390 Surfactant are speculative, at best. Also, note that DOWFAX 8390 Surfactant will be ionized in solution due to the low pKa of the sulfonate groups (estimated pK_a <2 [4]). Therefore, partitioning from water to air (i.e. volatilization) or from water to organic phases (i.e. octanol/water partition coefficient) may be significantly less than that predicted for the neutral (uncharged) molecule.

REFERENCES

1. Mackay, D. (2001). Multimedia Environmental Models: The Fugacity Approach. Lewis Publishers, CRC Press, Boca Raton, Florida. Models available at: http://www.trentu.ca/cemc/models.html
2. IUCLID Data Set for DOWFAX 8390 Surfactant. December 17, 2002.
3. U.S. EPA. 2000. EPIWIN software, version 3.11. United States Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D. C. Available at: http://www.epa.gov/oppt/exposure/docs/episuitedl.htm
4. Advanced Chemistry Development, Inc., Toronto, Canada. 2000. ACD/Log D. Version 4.56.
5. European Commission. (1996). Technical Guidance Documents in support of the commission directive 93/67/EEC on risk assessment for new notified substances and
commission regulation. European Commission, Brussels, Belgium.
6. Gonsior, S. J. and Markham, D. A. 1996. The Biodegradation of a Linear Monoalkylated (C16 Chain Length) Di-sulfonated Diphenyl Oxide Surfactant (MADS).
The Dow Chemical Company Report ES-2811.
7. Biodegradation of a Linear Monoalkylated (C16 Chain Length) Di-sulfonated Diphenyl Oxide Surfactant (MADS) in Aquatic Sediments. The Dow Chemical Company Report HET T3.02-000-000-304

Reliability : (2) valid with restrictions
2f: Accepted calculation method

13.06.2006

3.3.2 DISTRIBUTION

Media : water - soil
Method : other (measurement): OECD Guideline 106
Year : 1995
Method : For the investigation of the adsorption behavior three different soils were used: (I)strong silty sand (pH 4.0, 6.0% clay, 1.4% organic matter), (II)strong sandy loam (pH 7.5, 13.6% clay, 1.8% organic matter) and (III)weak sandy clay (pH 6.0, 17.8% clay, 1.35% organic matter). The soils were first equilibrated with water. To 2 g of each equilibrated soil 10 ml of an aqueous solution of the test material (Dowfax* 8390-D) (94.4 mg/l in 0.01 M CaCl2) was added. The following two controls were included: CaCl2 solution without test compound and test solution without soil. Incubation took place at room temperature with gentle tumbling over a period of 16 hours. Subsequently, the vials were centrifuged (5 min., 170 x g) and the supernatants pipetted off. The amount of residual test material still present in the supernatant after incubation (adsorption test) was analyzed with the halp of HPLC. To follow the desorption of the test material 10 ml of 0.01 M CaCl2 solution was added to the treated soil samples. The vials were again tumbled for 16 hours at room temperature

followed by centrifugation (5 min., 170 x g) and HPLC analysis of the supernatants.

This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland

Result : Dowfax 8390-D surfactant attained 99.0, 99.5, and 99.2% adsorption to soil I, II and III, respectively; the corresponding values have been determined to be 1.2, 0.5 and 0.8%. These data correspond to the K'oc values (adsorption coefficients as a function of the organic carbon content of the soils) of 392x10 2, 618x10 2 and 509x10 2 for soil type I, II and III, respectively.

Test substance : Test material for this test was XD 8390-D, the dry powder version of the product.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

26.04.2002 (7)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : domestic sewage
Concentration : 1mg/l related to Test substance
5mg/l related to Test substance
Contact time : 28 day
Degradation : <= 6 % after 28 day
Result : under test conditions no biodegradation observed
Deg. Product :
Method : Directive 84/449/EEC, C.6 "Biotic degradation - closed bottle test"
Year : 1990
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : The ready biodegradability of Dowfax 8390 was evaluated with the closed bottle test at concentrations of 1.0 and 5.0 mg/l. The test material was incubated for 28 days in an aerobic, aqueous medium which was inoculated with secondary effluent from a municipal sewage treatment plant. A 2 mg/l solution of sodium acetate served as a positive control. Oxygen concentration was determined at the start of the experiment and at days 5, 15 and 28, in duplicate. Degradation was calculated as the ratio of the biochemical oxygen demand to the chemical oxygen demand.
Result : Incubation of Dowfax 8390 at 1.0 or 5.0 mg/l for 28 days resulted in 0% and 6% biodegradation, respectively. The same conditions resulted in more than 88% degradation of the sodium acetate control. Thus, Dowfax 8390 appears not to be readily biodegradable under the conditions of the closed bottle test.
Test condition : Temperature medium (after aeration): 20.2C
)2-concentration of test medium (after aeration): 0.35 mg O2/l
pH values of different stock solutions: 7.6-7.8
Temperature of different stock solutions: 20.2C
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
15.08.2002 (8)

Type : aerobic
Inoculum : other: combined activated municipal and industrial sludge and soil microorganisms
Concentration : 22.3mg/l related to DOC (Dissolved Organic Carbon)

		20.83mg/l related to DOC (Dissolved Organic Carbon)
Contact time	:	28 day
Degradation	:	= 54 % after 28 day
Result	:	inherently biodegradable
Deg. Product	:	
Method	:	Directive 87/302/EEC, part C, p. 99 "Biodegradation: Zahn-Wellens test"
Year	:	1996
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Dowfax 8390 was at a 22.30 mg/l nominal DOC concentration. MADS was at a 20.83 mg/l nominal DOC concentration. Aniline and LAS were positive controls. Aniline/Dowfax mix was also tested. Samples of the reaction mixtures were removed for DOC analysis on days 0 (2.5hrs), 1,2,3,5,9,14,21,27 and 28.
Result	:	45% of the dissolved organic carbon (DOC) of MADS and 54% of the DOC of the commercial product Dowfax 8390 (of which MADS is a major component) were removed by biodegradation, which classifies both materials as inherently biodegradable.
Reliability	:	(1) valid without restriction

26.04.2002 (9)

Type	:	aerobic
Inoculum	:	other: surface soil
Concentration	:	2mg/l related to Test substance 20mg/l related to Test substance
Contact time	:	
Degradation	:	> 95 % after 4 day
Result	:	
Deg. Product	:	yes
Method	:	other
Year	:	1996
GLP	:	yes
Test substance	:	other TS
Method	:	Microcosms (100-ml serum bottles) containing the subsurface soil were prepared with 20 g of soil and 20 ml of a synthetic groundwater at pH 7.5. The soil/water mixtures were amended with [14C]MADS at concentrations of 2 and 20 ppm. Microcosms containing the surface soil were prepared with 24 g of soiland 16 ml of water. The soil/water mixtures were amended with [14C]MADS at concentrations of 2 and 20 ppm. Microcosms were sparged with oxygen before sealing and then incubation at 99 and 85 days, respectively. Duplicate microcosms were periodically sacrificed and analyzed (by LSC) to determine the concentrations of [14C]MADS and [14C]products. Distribution between parent and products was determined by PIC-HPLC. Selected microcosms were acidified, sparged with N2 and used to collect 14CO2 in traps with NaOH. Radioactivity in traps was quantified by LSC.
Result	:	Primary biodegradation (>95%) of 2 and 20 ppm [14C]MADS occurred within 4 days in a surface sandy loam soil. After 85 days, mineralization to 14CO2 ranged from 12% (20 ppm) to 29% (2 ppm) of the initial radioactivity. In the subsurface soil, primary biodegradation of 2 and 20 ppm [14C]MADS occurred within 10 and 30 days, respectively. Mineralization of [14C]MADS to 14CO2 was <1% after 99d days. A disulfodiphenyloxide carboxylate was identified as a major product in both soils.

Test substance	:	The test substance was identified as a linear monoalkylated (C16 Chain length) Di-sulfonated Diphenyl Oxide Surfactant (MADS). This was synthesized as the 14C-labeled material--uniformly labeled on the disubstituted ring.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (9)

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Concentration	:	20mg/l related to Test substance related to
Deg. Product	:	
Method	:	other: Soap & Detergent Assoc. Confirming Test (Semi-continuous activated sludge)
Year	:	1977
GLP	:	no
Test substance	:	other TS
Method	:	Surfactant concentrations in the test were analyzed by the methylene blue, chloroform extraction method. Absorbance of the chloroform extracts were determined on a P-E Spectophotometer. The apparent LAS concentration is calculated from the absorbance measured. Return activated sludge was collected from the north basin of the E. Lansing, MI, WWTP for the inoculum. The units were run in duplicate. The sludge was acclimated and equilibrated for 8 days, up to the operational level of 20 mg/l of test and control surfactant. Aeration was maintained at 500 ml/min. Each day, 1 l of effluent was removed for analysis.
Result	:	Apparent biodegradability for an average of 7 days operation: XD 8390-1 (early production) 87.70% (failed to pass 90% min) XD-8390-2 (late production) 92.99% (passed) XD 8390 composite 95.35% (passed) LAS control 99.10% Analysis by HPLC indicated that biodegradability varied inversely with a peak identified as indicative of the presence of Dowfax 2A1.
Test substance	:	Three samples of Dowfax 8390 were used: Early production Late production Composite
Reliability	:	(2) valid with restrictions

26.04.2002 (10)

Type	:	aerobic
Inoculum	:	other: river water and sediments
Concentration	:	1mg/l related to Test substance related to
Contact time	:	7 day
Degradation	:	ca. 89 % after 7 day
Result	:	
Deg. Product	:	
Method	:	other: biodegradation in river water and sediments under varying redox conditions
Year	:	1999
GLP	:	yes
Test substance	:	other TS
Method	:	The biodegradation of a linear, monoalkylated (C16 chain length), di-sulfonated diphenyl oxide surfactant (MADS) was evaluated in an aquatic sediment under different redox conditions. Reaction mixtures were prepared with river water and sediments, amended with 1 ppm

[14C]MADS, and incubated in the dark at 21 +/- 1C.

Separate reaction mixtures were incubated under aerobic conditions for 7 days to allow primary biodegradation of [14C]MADS to [14C]products to occur. Oxygen was depleted in the reaction mixtures and incubation continued under anaerobic (methanogenic) conditions.

Result : Approximately 89% primary biodegradation of [14C]MADS, defined as partial degradation of the aliphatic carbon side-chain, was observed within 7 days in aerobic sediment. Mineralization of [14C]MADS to 14C)2 reached 5% after 83 days, and 15% after 181 days. Little degradation of [14C]MADS occurred in killed control mixtures prepared with formalin, confirming that the mineralization observed was biologically mediated.

Anaerobic: Mineralization of the [14C]products to 14CO2 was less than 2% after 181 days. In addition, no degradation of [14C]MADS was observed in reaction mixtures maintained under anaerobic conditions throughout the study.

Test substance : The test substance was identified as a linear monoalkylated (C16 Chain length) Di-sulfonated Diphenyl Oxide Surfactant (MADS). This was synthesized as the 14C-labeled material--uniformly labeled on the disubstituted ring.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (9)

Type : aerobic
Inoculum : activated sludge, industrial
Concentration : 250mg/l related to Test substance
related to
Contact time : 8 day
Degradation : > 95 % after 8 day
Result :
Deg. Product :
Method : other: biodegradation of 14C MADS in activated sludge
Year : 1996
GLP : yes
Test substance : other TS
Method : Activated sludge from the Dow Chemical Company Michigan Division WWTP was acclimated to 1 mg/l MADS and several co-substrates structurally related to MADS (and known to be biodegradable) prior to the addition of 1 mg/l [14C]MADS.

The study lasted for 34 days. The reaction mixtures were maintained on a 3 or 4 day fill and draw cycle. The filtered supernatant was analyzed by HPLC.

Two days after the last additon of synthetic sewage, C14 MADS was added to each of the 5 reaction flasks at a conc. of 1 mg/l (18.9 microCi/flask). CO2 (caustic) traps were fitted on each reaction vessel.

Result : In both municipal and industrial activated sludge following extended exposure to MADS and biodegradable co-substrates, biodegradation of [14C]MADS proceded to [14C]products with little mineralization to 14CO2.

Test substance : C14 MADS [monoalkylated (C16 chain length), di-sulfonated diphenyl oxide surfactant] uniformly labeled on the di-substituted aromatic ring.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (11)

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 250mg/l related to Test substance
20mg/l related to Test substance

Contact time	:	8 day
Degradation	:	> 95 % after 8 day
Result	:	
Deg. Product	:	
Method	:	other: biodegradation of C14 MADS in activated domestic sludge (activated and non)
Year	:	1996
GLP	:	yes
Test substance	:	other TS
Method	:	The biodegradation of MADS in activated sludge was examined in 3 separate experiments: A: 2 to 250 mg/l [14C]MADS was added to activated sludge from the West Bay County WETP. No acclimation to MADS was attempted. B: Activated sludge from the same WWTP was acclimated to both 20 mg/l MADS and its biodegradation products prior to the addition of 2 and 20 mg/l [14C]MADS. C: Both municipal and industrial activated sludge were acclimated to 1 mg/l MADS and several co-substrates structurally related to MADS prior to addition of 1 mg/l [14C]MADS. (industrial activated sludge reported in separate record) One reaction solution from this experiment was used for direct analysis by LC-MS since it was likely to have the greatest amount of MADS products.
Result	:	In both municipal and industrial activated sludge following extended exposure to MADS and biodegradable co-substrates, biodegradation of [14C]MADS proceded to [14C]products with little mineralization to 14CO2. A disulfodiphenyloxide carboxylate was identified as the major product.
Test substance	:	C14 MADS [monoalkylated (C16 chain length), di-sulfonated diphenyl oxide surfactant] uniformly labeled on the di-substituted aromatic ring.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (11)

Type	:	aerobic
Inoculum	:	other: subsurface soil
Concentration	:	2mg/l related to Test substance 20mg/l related to Test substance
Contact time	:	
Degradation	:	> 95 % after 10 day
Result	:	
Deg. Product	:	yes
Method	:	other: biodegradation of C14 MADS in subsurface soil
Year	:	1996
GLP	:	yes
Test substance	:	other TS
Method	:	Microcosms (100-ml serum bottles) containing the subsurface soil were prepared with 20 g of soil and 20 ml of a synthetic groundwater at pH 7.5. The soil/water mixtures were amended with [14C]MADS at concentrations of 2 and 20 ppm. Microcosms containing the surface soil were prepared with 24 g of soiland 16 ml of water. The soil/water mixtures were amended with [14C]MADS at concentrations of 2 and 20 ppm. Microcosms were sparged with oxygen before sealing and then incubation at 99 and 85 days, respectively. Duplicate microcosms were periodically sacrificed and analyzed (by LSC) to determine the concentrations of [14C]MADS and [14C]products. Distribution between parent and products was determined by PIC-HPLC. Selected microcosms were acidified, sparged with N2 and used to collect 14CO2 in traps with NaOH. Radioactivity in traps was quantified by
Result	:	Primary biodegradation (>95%) of 2 and 20 ppm [14C]MADS occurred

within 4 days in a surface sandy loam soil.

After 85 days, mineralization to 14C)2 ranged from 12% (20 ppm) to 29% (2 ppm) of the initial radioactivity.

In the subsurface soil, primary biodegradation of 2 and 20 ppm [14C]MADS occurred within 10 and 30 days, respectively.

Mineralization of [14C]MADS to 14CO2 was <1% after 99d days.

A disulfodiphenyloxide carboxylate was identified as a major product in bot

Test substance : The test substance was identified as a linear monoalkylated (C16 Chain length) Di-sulfonated Diphenyl Oxide Surfactant (MADS). This was synthesized as the 14C-labeled material--uniformly labeled on the disubstituted ring.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (9)

Type : aerobic
Inoculum : other: microorganisms isolated from activated sludge and soil
Deg. Product :
Method : other: biodegradation with microorganisms originating from different sources under C- and N-limitation
Year : 1998
GLP :
Test substance : as prescribed by 1.1 - 1.4
Method : This is a preliminary study.

In a first assay, aqueous solutions of Dowfax* 8390 at concentrations ranging from 0.1 to 0.3 mM were passed through a trickling filter device inoculated with microorganisms isolated from activated sludge and soil.

Result : Microbial growth could be observed leading to suppression of effluent foaming and to degradation products which showed an increased polarity in HPLC whereas the UV chromatogram remained unchanged. It was concluded that alkyl chain shortening with no desulfonation would best explain these characteristics. An interesting observation was made indicating that growth only can take place in the presence of a polyester fleece (microorganisms using Dowfax 8390 as C-source seem to grow preferable on suitable surfaces).at

The eluate of the AM trickling filter experiment was treated with solid phase extraction and further purified from residual sulfate. Enrichment cultures growing on this purified eluate as the sole source of sulfur yielded degradation products with increased hydrophobicity and an unchanged UV spectrum which was interpreted as the result of desulfonation leaving the ring system intact. It is expected that desulfonation is a prerequisite for the later ring opening thus finally leading to complete mineralization of the product as has been observed in soil samples.

Reliability : (2) valid with restrictions
Flag : Material Safety Dataset
26.04.2002 (12)

Type : aerobic
Inoculum : activated sludge, domestic
Concentration : 20.3mg/l related to Test substance
related to
Contact time : 24 hour(s)
Degradation : > 97 % after 24 hour(s)
Result :
Deg. Product : yes
Method : other: generation of biodegradation products for use in aquatic toxicity tests

Year	:	1996
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Activated sludge from a municipla wastewater treatment plant was maintained in 3 semi-continuous activated sludge (SCAS) units fed synthetic sewage on a 24-hour treatment cycle. Two SCAS units were fed only synthetic sewage to provide control effluent while the third unit was fed synthetic sewage amended with 20.3 mg/l (34 micromoles/l) Dowfax 8390 surfactant to provide effluent containing biodegradation products of the surfactant. Previous studies showed that Dowfax 8390 surfactant biodegraded to primarily disulfodiphenyloxide carboxylates.
Result	:	Reverse phase HPLC analyses of the activated sludge mixed liquor dosed with the test material at the beginning and end of a treatment cycle confirmed >97% degradation of the Dowfax 8390 surfactant. Clarified effluents from the SCAS units were collected in 3 separate composite samples over a 4-day period. Analysis of the 3 composite effluents demonstrated that residual concentrations of Dowfax 8390 surfactant were less than 0.05 mg/l. Strong anion exchange HPLC confirmed the rpesence of the biodegradation products of Dowfax 8390 surfactant in the composite effluent from the SCAS unit fed the surfactant, at an estimated concentration of 16 mg/l (34 micromoles/l). The chromatographic profile of the biodegradation products was consistent with that of a disulfodiphenyloxide carboxylate, previously identified as a degradation product of a major component of Dowfax 8390 surfactant.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (13)

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Concentration	:	20mg/l related to Test substance related to
Contact time	:	24 hour(s)
Degradation	:	> 99 % after 24 hour(s)
Result	:	
Deg. Product	:	yes
Method	:	other: generation of biodegradation products for use in aquatic toxicity tests
Year	:	2000
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Activated sludge from a municipal wastewater treatment plant (Midland, MI) was maintained in two semi-continuous activated sludge (SCAS) units fed synthetic sewage on a 24-hour treatment cycle. One SCAS unit was fed sewage amended with 20 mg/l Dowfax 8390 surfactant to provide a test effluent containing biodegradation products of the surfactant, while the second unit was fed only synthetic sewage to provide a control effluent lacking surfactant or degradation products. Clarified effluents from each SCAS unit were collected as separate composite samples over a 5-day period.
Result	:	Primary biodegradation of Dowfax 8390 surfactant was observed in the SCAS unit fed the surfactant. Residual concentrations of Dowfax 8390 surfactant in the composite effluent were determined to be less than 0.18 mg/l, thus demonstrating greater than 99% removal of the parent surfactant in the activated sludge. HPLC and dissolved organic carbon analyses confirmed the presence of the biodegradation products of the surfactant in the composite effluent from the SCAS unit fed the surfactant, at an estimated concentration of 16 mg/l (33 micromoles/l). The chromatographic profiles of the biodegradation products were consistent with that of disulfodiphenyloxide carboxylates, previously identified as degradation products of a major component of Dowfax 8390 surfactant.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (14)

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Concentration	:	20mg/l related to Test substance related to
Contact time	:	
Degradation	:	ca. 95 % after 7 day
Result	:	
Deg. Product	:	
Method	:	other: semi-continuous activated sludge test from J. Am. Oil Chemists Soc., 1965.
Year	:	1974
GLP	:	no
Test substance	:	other TS
Method	:	Surfactant concentrations in the test were analyzed by the methylene blue chloroform extraction test. The transmittance of the chloroform extracts were determined on a Beckman Spectrophotometer; from this value, the apparent LAS is calculated. Settled, activated sludge from the E. Lansling, MI, WWTP was used as the inoculum. Duplicate aeration units were run for each sample to be tested, the LAS control and blank. The sludge, after being charged into the aeration unit was acclimated over 4 days, up to the operational level of 20 mg/l of test and control surfactant. Daily, each unit was fed 10 ml of synthetic sewage solution to sustain required 2500 mg/l suspended solids. Aeration was maintained at 500 ml/min over the 23 hr daily test period. Each day, a 1 l aliquot of the effluent liquid was removed from each unit for analysis.
Result	:	Biodegradation for an average of 7 days operation: XD 8390 (Lot 10154) 95.84% XD 8390 (Lot 09254) 94.47% 1:128 L&F 98.13% 1:256 L&F 98.47% LAS 99.14% Tube 4 containing 8390, lot 09254, on the 4th day of operation failed to pass the, "difference in percent removal of surfactant on any two consecutive days must not be more than 5%" (test requirement) The positive control, LAS was confirmed > required 97.5%. Dowfax XD 8390 met the SDA test requirements of >90% for biodegradability. The L&F samples also met the test requirements for biodegradability of >90%.
Test substance	:	Two lots of XD 8390 were used in the test (along with 2 disinfectant formulations from Lehn & Fink Products Co.).
Reliability	:	(2) valid with restrictions

26.04.2002 (15)

Type	:	anaerobic
Inoculum	:	
Concentration	:	1mg/l related to Test substance related to
Contact time	:	
Degradation	:	ca. 0 % after 7 day

Result	:	
Deg. Product	:	
Method	:	other: biodegradation in river water and sediments under varying redox conditionsbiodegradation of radiolabeled surfactant in river water and sediments
Year	:	1999
GLP	:	yes
Test substance	:	other TS
Method	:	The biodegradation of a linear, monoalkylated (C16 chain length), di-sulfonated diphenyl oxide surfactant (MADS) was evaluated in an aquatic sediment under different redox conditions. Reaction mixtures were prepared with river water and sediments, amended with 1 ppm [14C]MADS, and incubated in the dark at 21 +/- 1C. Separate reaction mixtures were incubated under aerobic conditions for 7 days to allow primary biodegradation of [14C]MADS to [14C]products to occur. Oxygen was depleted in the reaction mixtures and incubation continued under anaerobic (methanogenic) condition
Result	:	Approximately 89% primary biodegradation of [14C]MADS, defined as partial degradation of the aliphatic carbon side-chain, was observed within 7 days in aerobic sediment. Mineralization of [14C]MADS to 14C)2 reached 5% after 83 days, and 15% after 181 days. Little degradation of [14C]MADS occurred in killed control mixtures prepared with formalin, confirming that the mineralization observed was biologically mediated. Anaerobic: Mineralization of the [14C]products to 14CO2 was less than 2% after 181 days. In addition, no degradation of [14C]MADS was observed in reaction mixtures maintained under anaerobic conditions throughout the stud
Test condition	:	The pH of the River water sediment was 8.0 and it contained 0.5% organic matter
Test substance	:	The test substance was identified as a linear monoalkylated (C16 Chain length) Di-sulfonated Diphenyl Oxide Surfactant (MADS). This was synthesized as the 14C-labeled material--uniformly labeled on the disubstituted ring.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

15.08.2002 (9)

3.6 BOD5, COD OR BOD5/COD RATIO

COD		
Method	:	other: acidic dichromate digestion procedure (Hach)
Year	:	1987
GLP	:	yes
COD	:	= 2.24 mg/g substance
Result	:	The resulting COD is calculated on a 100% active basis. COD (part of oxygen/part of product) =2.24.
Test substance	:	XDS 8390.00 was 35% active ingredient in water.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (16)

3.7 BIOACCUMULATION

Elimination	:	
Method	:	other: OECD Guidelines for determination of fat solubility EEC Directive 84/449

Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	A commercially available standard fat (HB 307) was used. This fat silulant is a synthetic mixture of saturated triglycerides with a fatty acid and triglyceride distribuiton similar to that of a coconut fat. The density of the standard fat was measured to be 0.91 g/cm3. Approx. 109 g test substance was dried for approx 10 hrs in a rotary evaporator. The residue was put in a stove for 4 days at 60 C, resulting in a dry brown powder. This was ground and weighed 40.6 g. This ground material was put on a petri dish and dried in the stove for another 26 hrs at 60 C. The remaining off-white powder was used for the fat solubility determination. A preliminary range-finding test was conducted. 102 mg of test substance was added to 100 ml standard fat and shaken in a water bath at 37C for aobut 16 hrs. A 5 ml sample of the fat was taken and accurately weighed. This sample was mixed with Milli-Q water for 2 minutes; the mix was refrigerated to solidify the fat; the clear water phase was diluted 5X with more Milli-Q water using variable volume pipettes and volumetric flasks; the concentration of the test substance in the diluted water sample was determined spectrophotometrically at 235 nm. A recovery experiment and blank were performed. Recoveries were low and results were not reproducible. Modifications were made without success. Thus, the main experiment was conducted with a very low concentration of test substance in fat. Four Erlenmeyer flasks were used for the test. approx. 10 mg test substance and 100 ml of liquefied and mixed standard fat were added to each. The flasks were tichtly closed; two were shaken in a water bath at 30 C and two at 50 C for one hour; all 4 flasks were then placed in a bath at 37C and stirred for 3 hrs; let rest for 30 minutes; observations of consistency made; returned to bath at 37C and stirred for another 20.5 hrs; rested for 1.5 hrs to equilibrate; another observation for consistency made; flasks left to rest 20 more hours and then observed again. The observations were for finding traces of the solid undissolved material.
Result	:	After each of the 3 observations, there was still solid test material observed in the flasks. It was concluded that the test substance did not dissolve in standard fat at the concentration tested. A lower concentration could not be tested due to the limitations of the visual observations. From this, a maximum solubility of test substance in standard fat of <95 mg/1000 ml at a temperature of 37C was calculated.
Test substance	:	The test substance was Dowfax 8390 containing 36.7% active ingredient in water. The water was evaporated prior to the test.
Reliability	:	(1) valid without restriction
Flag	:	Risk Assessment

26.04.2002 (17)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Oncorhynchus mykiss (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
Method	:	other: 40 CFR part 792
Year	:	1996
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Samples of activated sludge effluent were prepared in semi-continuous activated sludge (SCAS) units in the Environmental Chemistry Research Lab, Health and Environmental Sciences, The Dow Chemical Company. Synthetic sewage amended with 20 mg/l Dowfax 8390 surfactant (nominal conc) was treated with municipal activated sludge to generate the biodegradation products. Effluents were provided from 3 SCAS units, designated Unit A, Unit B, and Unit C. Unit A was a post-treatment blank effluent with nominal treatment levels to the test organisms of 6.25, 12.5, 25.0, 50.0 and 100.0%. Unit B was the post-treatment blank effluent levels amended with Dowfax 8390 with nominal concentrations of 0.125, 0.25, 0.5, 1.0 and 2.0 mg/l for rainbow trout and 1.25,2.5, 5.0, 10.0,, and 20.0 mg/l for the daphnid. Unit C was the post-treatment Dowfax 8390 biodegradation product with nominal treatment levels of 6.25, 12.5, 25.0, 50.0 and 100.0% which corresponds to initial concentrations of Dowfax 8390 of 1.25, 2.5, 5.0, 10.0 and 20.0 mg/l. Both studies for the rainbow trout (96 hr) and daphnid (48 hr) were designed as static tests with replicate groups of 10 organisms exposed to each nominal concentration.
Result	:	Rainbow Trout-Unit A and C: LC50 >100% with 95% CI >100% EC50 >100% with 95% CI >100% Rainbow trout-Unit B: Nominal concentration of Dowfax 8390 LC50 0.7 mg/l (0.5-1.0, 95% CI) EC50 0.7 mg/l (0.5-1.0, 95% CI)
Test condition	:	Water Quality Measurements Laboratory water (Rainbow trout: Hardness (as CaCO3) 68 Alkalinity 40 Conductivity 240 pH 7.6 Chlorine 5.0 Daphnid water (Daphnid): Hardness (as CaCO3) 180 Alkalinity 45 Conductivity 540 pH 8.1 Chlorine <1 Test Vessel Data Rainbow trout: Temperature range (deg C) 11.6-12.3 pH range 7.0-7.6 Dissolved Oxygen (mg/L) 7.2-11.3 (>70% saturation) Daphnid: Temperature range (deg C) 19.6-20.9 pH range 7.3-7.7 Dissolved Oxygen (mg/L) 7.8-9.6 (>88% saturation) Light Intensity (lux) 2142 +/- 171.5

Conclusion	:	The non-amended effluent control (Unit A) had no effects on the rainbow trout. However, modified effluent in Unit B elicited toxicity to the trout, demonstrating that Dowfax 8390 added directly to the effluent caused toxicity, where the biodegradation products from activated sludge treatment of Dowfax 8390 (Unit C) did not.
Reliability	:	(1) valid without restriction

15.08.2002 (18)

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
Method	:	other: historic Dow test method
Year	:	1975
GLP	:	no
Test substance	:	other TS
Method	:	Two Lots, #09254 and #10154, of Dowfax XD-8390 were evaluated for static acute fish toxicity with fathead minnows (Pimephales promelas Rafinesque). Groups of ten minnows were exposed to five concentfrations of the toxicant (0.36, 0.603, 1.00, 1.67 and 2.79 mg/l--as 35% active) in ten liters of Lake Huron water at 10C for 96 hours. A control exposure with fish, but without toxicant, was included to provide a measure of the health of the test fish and quality of dilution waters.
Result	:	Lot 09254 (mg/l active ingredient) NOEC: <0.36 Partial Kill: 0.36 100% Lethal: 1.67 LC50: 0.86 LOt 10154 (mg/l active ingredient) NOEC: 0.36 Partial Kill: 0.60 100% Lethal: 1.67 LC50: 1.03
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (19)

Type	:	static
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
NOEC	:	m = .1
LC50	:	c = .42
LC100	:	m = 1
EC50	:	c = .36
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	This study was carried out at the request of Dow Chemical Europe, Horgen, Switzerland. Rainbow trout with a length of about 5 cm are exposed to various concentrations of the test material (0.1, 0.18, 0.32, 0.56, 1.0, 1.8 and 3.2 mg/l) for 96 hrs. Effects were recorded at 24-hr intervals. A range-finding test using 5 fish/dose determined doses for the acute test. Ten fish per dose were used in the acute test (6 fish in 17 l aquarium and 4 fish in 12 l aquarium). All solutions were prepared within 4 hrs of use.
Test condition	:	During the final acute test, the Ph ranged from 8.1 to 8.4 between 0 hours

and 96 hours in the various test concentration vessels. Likewise, the pO2 levels were between 7.5 and 9.2 mg/l.

Conclusion : It was concluded, based on this study, that XD 8390 has high toxicity to fish.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
15.08.2002 (20)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no
Method : other: 40 CFR Part 792
Year : 1996
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : Samples of activated sludge effluent were prepared in semi-continuous activated sludge (SCAS) units in the Environmental Chemistry Research Lab, Health and Environmental Sciences, The Dow Chemical Company. Synthetic sewage amended with 20 mg/l Dowfax 8390 surfactant (nominal conc) was treated with municipal activated sludge to generate the biodegradation products. Effluents were provided from 3 SCAS units, designated Unit A, Unit B, and Unit C. Unit A was a post-treatment blank effluent with nominal treatment levels to the test organisms of 6.25, 12.5, 25.0, 50.0 and 100.0%. Unit B was the post-treatment blank effluent levels amended with Dowfax 8390 with nominal concentrations of 0.125, 0.25, 0.5, 1.0 and 2.0 mg/l for rainbow trout and 1.25,2.5, 5.0, 10.0,, and 20.0 mg/l for the daphnid. Unit C was the post-treatment Dowfax 8390 biodegradation product with nominal treatment levels of 6.25, 12.5, 25.0, 50.0 and 100.0% which corresponds to initial concentrations of Dowfax 8390 of 1.25, 2.5, 5.0, 10.0 and 20.0 mg/l. Both studies for the rainbow trout (96 hr) and daphnid (48 hr) were designed as static tests with replicate groups of 10 organisms exposed to each nominal concentration.
Result : Daphnid-Unit A and C:
LC50 >100% with 95% CI >100%
EC50 >100% with 95% CI >100%

Daphnid-Unit B: Nominal conc. of Dowfax 8390
LC50 14.1 mg/l (11.6-18.2, 95% CI)
EC50 13.5 mg/l (11.1-17.3, 95% CI)
Test condition : Water Quality Measurements
Laboratory water (Rainbow trout:
Hardness (as CaCO3) 68
Alkalinity 40
Conductivity 240
pH 7.6
Chlorine 5.0
Daphnid water (Daphnid):
Hardness (as CaCO3) 180
Alkalinity 45
Conductivity 540
pH 8.1
Chlorine <1

Test Vessel Data
Rainbow trout:
Temperature range (deg C) 11.6-12.3

pH range 7.0-7.6
Dissolved Oxygen (mg/L) 7.2-11.3 (>70% saturation)
Daphnid:
Temperature range (deg C) 19.6-20.9
pH range 7.3-7.7
Dissolved Oxygen (mg/L) 7.8-9.6 (>88% saturation)
Light Intensity (lux)

Conclusion : The non-amended effluent control (Unit A) had no effects on the daphnia. However, modified effluent in Unit B elecited toxicity on both organisms, demonstrating that Dowfax 8390 added directly to the effluent caused toxicity, where the biodegradation products from activated sludge treatment of Dowfax 8390 (Unit C) did not.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
15.08.2002 (18)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no
NOEC : m = 5.6
EC50 : c = 13.9
LC100 : m = 56
Method : other: stated as OECD Method 202, 1984 ?
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : The study was carried out at the request of Dow Chemical Europe, Horgen, Switzerland.

To assess the acute toxicity of the test material, less than 48 hrs old Daphnia are exposed to various concentrations of the test material (1.0, 1.8, 3.2, 5.6, 10, 18 32 and 56 mg/l) for 48 hrs. Immobility is then scored. About 250 Daphnia were placed into 10 liters of DSW in each of 2 glass vessels. The test was performed in duplicate. A range-finding test in 10 Daphnia determined final concentrations.
Test condition : The DSW water had 84.8 mg/l HCO3 right after preparation, hardness was 11.7 deg DH, and the pH was 8.2.

During the final test, 0 hour pH ranged from 8.2 to 8.3 and pO2 ranged from8.6 to 8.8 mg/l. At 48 hours, the pH ranged from 8.2 to 8.3 and the pO2 ranged from 8.6 to 8.8 in the various concentration vesses.
Conclusion : It was concluded that XD 8390 has low toxicity to Daphnia magna, based on this study.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
15.08.2002 (21)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint : growth rate
Exposure period : 72 hour(s)
Unit : mg/l
Analytical monitoring : yes
NOEC : c = 10
NOEC (inhibition of biomass formation) : c < 10
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"

Year	:	1995
GLP	:	yes
Test substance	:	other TS
Method	:	Subsequent to a range-finding study the cells of S. capricornutum were exposed to triplicate samples of an aqueous nutrient solution (approx. 50 ml) containing 10, 18, 32, 56 and 100 mg/l of the test material over a period of 72 hrs. Additional 6 parallel samples were included as blank controls without addition of the test material. Furthermore, one sample with the highest test substance concentration without algae was incubated. The incubation took place on a laboratory shaker under continuous illumination (7000-8000 lux). Samples of the algae suspensions were taken at 24, 48 and 72 hours and the cell number was determined by turbidity measurements with the use of a spectrophotometer at 720nm. The area under the growth curve and the growth rates were used as a base for the calculation of the concentration leading to 50% growth inhibition: EbC50 and ErC50 referring to the area under the growth curve (biomass) and to the growth rate, respectively. The study was conducted for Dow Chemical Europe, Horgen, Switzerland.
Result	:	The nominal effective 72-hr EbC50 of Dowfax 8390-D surfactant tested with S. capricornutum was 42 mg/l (95% confidence interval 30-68 mg/l). The EC50 value for growth rate reduction (ErC50: 0-72h) was beyond the test concentrations assayed. The NOEC for growth rate reduction and inhibition of biomass formation was 10.0 and <10.0 mg/l, respectively.
Test condition	:	Test medium pH was 0.24 mmol/l (24 mg CaCO3/l). pH levels during the final study were 8.3 in each vessel at the beginning and end.
Test substance	:	The test material was the dry powder material.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

15.08.2002 (22)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	activated sludge, domestic
Exposure period	:	30 minute(s)
Unit	:	mg/l
Analytical monitoring	:	no
EC50	:	c > 284
Method	:	OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year	:	1995
GLP	:	yes
Test substance	:	other TS
Method	:	The effect of the test material on the respiration rate of activated sludge from a municipal waste water treatment plant was determined by comparing the oxygen consumption of samples treated with 5 different concentrations of the test material (25, 50, 100, 200 and 284 mg/l) with two untreated control samples (oxygen determination at the start and at the end of the experiment). The oxygen consumption was measured with an oxygen electrode after an incubation period of 30 minutes at 20C. The susceptibility of the activated sludge was evaluated by the addition of 3,5-dinitrophenol (3.2, 10.0 and 32.0 mg/l).
Result	:	The test substance showed a slight inhibitory effect on aerobic waste water bacteria, the inhibition ranging from 11 to 25% at 25 and 200 mg/l, respectively. Since the slowly increasing inhibitory effect seemed to level-off at the highest concentration tested (only 26% inhibition at 284 mg/l) the EC50 value for Dowfax 8390-D surfactant could not be determined (EC50 > 284 mg/l). The control with 3,5-dinitrophenol showed an EC50 value of 6 mg/l indicating suitability of the test conditions.
Test condition	:	The pH of the synthetic sewage feed was 7.1 and the medium temperature

was 20C. Milli-Q water was used.

Test substance : The test material was Dowfax 8390-D surfactant (the dry powder material).
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
15.08.2002 (23)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species : Daphnia magna (Crustacea)
Endpoint : other: survival, reproduction, growth
Exposure period : 21 day
Unit : mg/l
Analytical monitoring : yes
Method : other: OECD Method 211: Daphnia magna Reproduction Test. Adopted 9/21/98.
Year : 2001
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Result : Daphnid Survival:
Survival in the DDW control and in all effluent treatments was >/= 80%. No significant differences in survival were observed between any test treatment and the culture water control.

Daphnid Reproduction:
The mean number of young produced in each effluent treatment (Dowfax 8390 surfactant-amended or unamended) was not significantly less than the mean number of young produced by daphnids in culture water. The coefficient of variation for reproduction of DDW control animals was 19.5%.

Daphnid Growth:
Growth of daphnia in each effluent treatment (Dowfax 8390 surfactant-amended or unamended) was not significantly reduced relative to growth of daphnids in culture water. Average length of D. magna in the culture water control was 3.9 +/- 0.28 mm, while the average length of daphnids in effluent treatments was 4.2 +/- 0.2 mm with a range of 3.8-4.4 mm.

Test condition : Static-renewal (48-hr renewal): 21-day exposure duration. Ten replicates per treatment, one Daphnia magna/ replicate. The pH of test solutions averaged 7.3+/-0.1 (range: 7.1-7.6). The dissolved oxygen concentration averaged 8.8 +/- 0.2 mg/l (range: 8.2-9.2 mg/l); oxygen saturation in test vessels remained above 91%. Temperatures during the exposure period averaged 20.1 +/- 0.3 C (range=19.3-20.9C). The light intensity averaged 61.8 +/- 15.3 ft-candles (range = 30-95 ft-candles), equivalent to 665 +/- 165 lux (range = 323-1023 lux).

0 (DDW control); 6.25, 12.5, 25.0, 50.0 and 100% activated sludge effluent amended with Dowfax 8390 surfactant. Control effluent solutions were prepared with 6.25, 12.5, 25.0, 50.0 and 100% activated sludge effluent to which Dowfax 8390 surfactant was not added.

Conclusion : In summary, Dowfax 8390 surfactant degradation products did not reduce survival, reproduction, or growth of Daphnia magna. These results indicate that the toxicity of Dowfax 8390 surfactant is removed during the wastewater treatment process.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (24)

Species	:	Daphnia magna (Crustacea)
Endpoint	:	reproduction rate
Exposure period	:	21 day
Unit	:	mg/l
Analytical monitoring	:	yes
NOEC	:	c = 1
NOEC	:	m = .7
Method	:	OECD Guide-line 202, part 2 "Daphnia sp., Reproduction Test"
Year	:	1996
GLP	:	yes
Test substance	:	other TS
Method	:	Daphnia were exposed to nominal concentrations of the test material of 0.22, 0.46, 1.0, 2.2, 4.6, and 10.0 mg/l in a semi-static system (renewal of the test medium 3-times per week). Individual neonate Daphnids were put into 100 ml glass vessels containing 50 ml test medium. Ten parallel samples per test material concentration were incubated. The non-treated control consisted of 20 neonate Daphnides which were also individually incubated. The vessels were kept at 20-22C and illuminated for 16 hrs/day (600 lux). These animals were fed with Chlorella pyrenoidosa suspensions. Analytical verifications of the test compound concentrations were performed with HPLC.
Result	:	Exposure of the Daphnids to 1.0 mg/l Dowfax 8390-D induced only a slightly lower number of living young as compared to the negative control--an effect which was considered to be statistically non-significant. Exposure to higher concentrations (2.2 - 10.0 mg/l) hardly produced any offspring whereas at 0.22 and 0.46 mg/l the reproductive capacity of the Daphnids was significantly stimulated. Based on these data the nominal 21-day No Observed Effect Concentration for reproduction and parental mortality (overall NOEC) was determined to be 1.0 mg/l whereas the corresponding measured value due to >20% decrease in the test compound concentration during the last 24 hrs of the 72 hr-semistatic exposure period was calculated to be 0.7 mg/l.
Test condition	:	After aeration the hardness of the medium M4 was 250 mg CaCO3/ l and the pH was 8.0. During the test, the pH ranged from 7.8-8.3. Oxygen concentrations as mg O2/l ranged from 7.1 to 9.5. The temperature of the medium ranged from 20.2 to 21.1 C.
Test substance	:	Dowfax 8390-D was used (that is the dry form of the product).
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

15.08.2002 (25)

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	5
Vehicle	:	water
Value	:	> 5000 mg/kg bw
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	1991
GLP	:	yes
Test substance	:	other TS
Method	:	Subsequent to a range-finding study, five male and five female Sprague-Dawley rats were given a single gavage dose of the test material as a solution in distilled water at a dose level of 5000 mg/kg body weight. Animals were observed at 0.5, 1, 2 and 4 hours after dosing and then once daily for 14 days. Individual body weights were recorded on the day of treatment and on days 7 and 14. Animals were examined for gross pathological changes at the termination of the study. The study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.
Result	:	There were no deaths. One male rat had a hunched posture at 4 hrs after dosing. No other clinical signs were noted. There were no significant effects on body weights during the study and there were no treatment-related post-mortem observations at the termination of the study. The acute, oral median lethal dose (LD50) of Dowfax 8390 surfactant was >5000 mg/kg in the S-D rat.
Test substance	:	The test material was a powdered (solid) sample of Dowfax 8390, with a purity of 91.6%.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (26)

Type	:	LD50
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: unduluted
Value	:	> 5000 mg/kg bw
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland. Dowfax* XD 8390 (primarily C-16 alkylated sodium sulfonated diphenyl oxide) was given undiluted by gavage to groups of 5 male and 5 female Wistar rats at a dose of 5000 mg/kg. The rats were observed immediately after dosing, at 2, 4, and 6 hrs after dosing and on days 1-6 and 14. The rats were weighed on days 0, 7 and 14 and were submitted for gross pathologic exams on day 14.
Result	:	There were no mortalities during the 14-day observation period. Although diarrhea and reduced defecation were noted, the weekly group mean body gain of these animals was normal.

No treatment-related macroscopic abnormalities were observed at necropsy.

Since there were no mortalities, the LD50 is estimated to be >5000 mg/kg.

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (27)

Type : LD50
Species : rat
Strain : Fischer 344
Sex : male
Number of animals : 3
Vehicle : other: undiluted commercial liquid
Value : > 2000 mg/kg bw
Method : other: Dow range-finding
Year : 1995
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : Three male F344 rats received 2000 mg/kg of neat Dowfax 8390 by single-dose oral gavage. The rats were weighed on days 1,2, 8 and 15.
Result : All rats survived the 14-day observation period. Fecal soiling and salivation were observed from 3 hours after dosing thfrough test day 3. Administration of Dowfax 8390 had no effect on body weight during the two week observation period. Therefore, under the conditions of this study, the estimated acute oral LD50 of Dowfax 8390 for male F344 rats was >2000 mg/kg.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
26.04.2002 (28)

Type : LD50
Species : rat
Strain : Fischer 344
Sex : female
Number of animals : 3
Vehicle : water
Value : ca. 1500 mg/kg bw
Method : other: Dow range-finding
Year : 1987
GLP : no
Test substance : other TS
Method : Three female Fischer 344 rats/dose were fed 20% aqueous solutions of XU-040341.00 by oral gavage in doses of 1000, 1500 and 2000 mg/kg. The rats were weighed on days 0, 1, 7 and 14 and were observed several times on day 0 and then daily on days 1-4, 7-11 and 14.
Result : Dead/Dose

1 dead/2000 mg/kg
1 dead/1500 mg/kg
0 dead/1000 mg/kg

Thus, the estimated LD50 for female F344 rats is 1500 mg/kg.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
26.04.2002 (29)

Type : LD50
Species : rat
Strain : Sprague-Dawley
Sex : female
Number of animals : 6

Vehicle	:	other: undiluted liquid dosed
Value	:	= 7744 mg/kg bw
Method	:	other: Dow range-finding
Year	:	1980
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of 6 female S-D rats/dose were fed the undiluted XD-8390 by oral gavage in doses of 1.3, 2.5, 5.0 10.0, 6.3 and 8.0 g/kg. The rats were weighed on days 0, 17 and 14. The rats were observed periodically the day of dosing and daily on weekdays until the end of the study. The survivors were submitted for gross necropsy at day 14
Result	:	Dose (g/kg) and deaths: 1.3 0/6 2.5 0/6 5.0 0/6 6.3 0/6 8.0 5/6 10.0 6/6 Following dosing, all rats were lethargic and had diarrhea. In addition, rats of the 5000, 6300, 8000 and 10,000 mg/kg groups had piloerection. Upon gross pathological examination 2 weeks post-treatment, rats of the 5000 mg/kg dose group had a slight, pale discoloration of the mucosal surface of the glandular portion of the stomach. This was not observed upon examination of surviving rats of the 6300 and 8000 mg/kg groups. All surviving rats gained weight during the 2-week post-treatment observation period.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

26.04.2002 (30)

Type	:	LD50
Species	:	rat
Strain	:	no data
Sex	:	female
Number of animals	:	3
Vehicle	:	other: undiluted liquid
Value	:	> 3980 mg/kg bw
Method	:	other: Dow range-finding
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Three female rats/dose were fed the undiluted liquid by oral gavage in doses of 252, 500, 1000, 2000 and 3980 mg/kg. The rats were weighed on days 0, 1, 7 and 14. They were observed daily for signs of toxicity. (No recording of effects unless it was 'something'.)
Result	:	There were no signs of toxicity other than 'slight urine soaked' on the day after dosing. There were no deaths. One rat of each dose was evaluated grossly at necropsy. There were no visible lesions except for some slight fecal abnormalities.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

26.04.2002 (31)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: undiluted
Value	:	> 2000 mg/kg bw
Method	:	OECD Guide-line 402 "Acute dermal Toxicity"
Year	:	1991
GLP	:	yes
Test substance	:	other TS
Method	:	Five Sprague-Dawley rats/sex were treated with a single, occluded, dermal application of the undiluted test material to the intact skin which was moistened with distilled water. The material was applied at a dose of 2000 mg/kg to an area of shorn skin which approximated 10% of the total body surface area. Twenty-four hours after application, the dressing and residual test material were removed. The rats were observed for signs of toxicity and death at 0.5, 1, 2 and 4 hours after dosing and subsequently at least once/day for 14 days. Body weights were recorded on the day of dosing and on days 7 and 14. The rats were examined for gross pathologic changes at the termination of the study. This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.
Result	:	There were no deaths, signs of systemic toxicity nor skin irritation. No significant effects on body weight were noted and there were no treatment-related post mortem observations at the termination of the study. The acute dermal median lethal dose (LD50) of Dowfax 8390 was >2000 mg/kg in the S-D rat.
Test substance	:	The test material was a powdered sample of Dowfax 8390, 91.6% pure.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (32)

Type	:	LD50
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	5
Vehicle	:	other: undiluted
Value	:	> 2000 mg/kg bw
Method	:	OECD Guide-line 402 "Acute dermal Toxicity"
Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Five Wistar rats/sex were treated with a single, occluded, dermal application of the undiluted test material to the intact skin. The material was applied at a dose of 2000 mg/kg to an area of shorn skin which approximated 10% of the total body surface area. Twenty-four hours after application, the dressing and residual test material were removed. The rats were observed for signs of toxicity and death immediately after dosing and at 2 and 4 hours and subsequently at least once/day for 14 days. Body weights were recorded on the day of dosing and on days 7 and 14. The rats were examined for gross pathologic changes at the termination of the study. This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerlan

Result	:	There were no deaths nor signs of systemic toxicity. The treated skin surface showed spots with erythema; these skin abnormalities disappeared during the second week of observations. No significant effects on body weight were noted and there were no treatment-related post mortem observations at the termination of the study. The acute dermal median lethal dose (LD50) of Dowfax 8390 was >2000 mg/kg in the Wistar rat.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (33)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	10 % active substance
Exposure	:	Occlusive
Exposure time	:	4 hour(s)
Number of animals	:	6
PDII	:	
Result	:	not irritating
EC classification	:	not irritating
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1997
GLP	:	yes
Test substance	:	other TS
Method	:	The day prior to study start, an area approximately 10 x 10 cm on the back of 9 male and 9 female New Zealand White rabbits, was clipped free of fur. On test day 1, a 0.5 ml aliquot of each respective test material was applied to an intact site on the backs of 6 rabbits/test material and covered with a gauze patch with cotton backing. The gauze patch was held in place with an elastic rabbit jacket. The jacket and patch were removed after 4 hours and the back was wiped with a damp disposable towel to remove any residue. The application sites were graded for erythema and edema within 30 minutes, 24, 48 and 72 hours, and when necessary, at 7 days after test material removal. Animals were weighed on the day of treatment and at study termination.
Result	:	There were no signs of dermal irritation of the test site in any of the 6 rabbits that were dosed with Dowfax 8390. In contrast, slight irritation was noted in several rabbits treated with the other two surfactants.
Test substance	:	The test material was a 10% aqueous solution prepared by the sponsor. Also tested, for comparison, were two other surfactants: VISTA C-550 SLURRY and STEOL CS-370 (also supplied as 10% aqueous solutions).
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (34)

Species	:	rabbit
Concentration	:	other: moistened with water
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	3
PDII	:	
Result	:	slightly irritating

EC classification	:	not irritating
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1991
GLP	:	yes
Test substance	:	other TS
Method	:	The day prior to study start, an area on the back of 1 female and 2 male New Zealand White rabbits, was clipped free of fur. On test day 1, 0.5 g of the test material was applied to an intact site on the backs of the rabbits and covered with a gauze patch with cotton backing. The gauze patch was held in place with an elastic rabbit corset. The corset and patch were removed after 4 hours and the back was wiped with a damp disposable towel to remove any residue. The application sites were graded for erythema and edema within 1, 24, 48 and 72 hours after test material removal. Animals were weighed on the day of treatment. This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.
Result	:	Very slight erythema was noted at the treatment site of all animals one hour after patch removal; the erythema persisted in two animals at the 24-hour observation and in one animal at the 48-hour observation. Very slight edema was noted at the treatment site of one animal only at the 1-hour observation. The treatment site of all animals appeared normal at the 72-hour observation. No corrosive effects were noted. The primary irritation index was 0.3 on a 1 to 8 scale and was classified as a slight irritant to rabbit skin according to the Draize classification scheme.
Test substance	:	The test material was the powdered/solid material, with a purity of 91.6%.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (35)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	3
PDII	:	
Result	:	slightly irritating
EC classification	:	not irritating
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The day prior to study start, an area approximately 10 x 10 cm on the back of 3 female New Zealand White rabbits, was clipped free of fur. A volume of 0.5 ml aliquot of the test material was applied to a 6 cm2 gauze patch, which was attached with a drop of petrolatum to aluminum foil and mounted on permeable tape. This was applied to the left flank of each animal, the right flank being covered with the same dressing without test material. Finally the rabbits were wrapped in flexible bandage. The wrappings and patch were removed after 4 hours and the flanks wiped dry and then moistened tissues. The application sites were graded for erythema and edema within 30-60 minutes, 24, 48 and 72 hours after test material removal. This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.
Result	:	Slight, immediate edema and erythema resulted from contact with the test substance; the erythema persisted for 2 days in 2 of the animals.
Test substance	:	The test material was Dowfax XD 8390, a brown liquid.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (36)

Species	:	rabbit
Concentration	:	other: undiluted commercial liquid
Exposure	:	Occlusive
Exposure time	:	2 day
Number of animals	:	1
PDII	:	
Result	:	highly irritating
EC classification	:	not irritating
Method	:	other: Dow range-finding
Year	:	1995
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The skin irritation test included topical application of neat Dowfax 8390 to the inner surface of the left ear (0.1 ml) (open) and to intact and abraded skin on the abdomen (0.5 ml each) of 1 male New Zealand White rabbit. Two applications were made and no more due to severe irritation.
Result	:	Very slight erythema was observed at both abdominal test sites, after one application. After two applications, slight erythema was observed at the intact abdominal test site, and severe erythema and burns were observed at the abraded abdominal test site. The test was terminated and the animal was humanely euthanized.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (28)

Species	:	rabbit
Concentration	:	other: applied dry in one rabbit and moistened with water on the other
Exposure	:	Occlusive
Exposure time	:	5 day
Number of animals	:	2
PDII	:	
Result	:	slightly irritating
EC classification	:	not irritating
Method	:	other: Dow range-finding
Year	:	1987
GLP	:	no
Test substance	:	other TS
Method	:	The skin irritation test included topical application of solid XU-040341.00 to intact and abraded skin on the abdomen (0.5 g each) of 2 male New Zealand White rabbits--one with dry applications and one with moistened (water). Five applications were made on the intact abdominal site and 3 to the abraded. No ear applications were made since the material is a powder. The rabbits were weighed on days 1 and 8.
Result	:	Under dry conditions, no irritation was seen. Under water-moistened conditions slight erythema was observed after prolonged and repeated contact. The dermal response was attributed to mechanical injury, since the test material appeared to glue the cotton patch to the skin when moisture was present, making removal difficult.
Test substance	:	The test material was the solid/powdered form of XD-8390, called XU-040341.00.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (29)

Species	:	rabbit
Concentration	:	other: undiluted commercial liquid (45% aqueous)
Exposure	:	Occlusive
Exposure time	:	10 day
Number of animals	:	1
PDII	:	
Result	:	slightly irritating

EC classification	:	not irritating
Method	:	other: Dow range-finding
Year	:	1980
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The skin irritation test included topical application of neat Dowfax 8390 to the inner surface of the left ear (0.1 ml) (open) and to intact and abraded skin on the abdomen (0.5 ml each) of 1 male New Zealand White rabbit. Ten daily applications were made to the ear and intact abdominal site and 3 to the abraded abdominal site. The rabbit was weighed on days 1, 7 14, and 23. It was evaluated daily on weekdays through day 14 and on day 23.
Result	:	Contact on confined rabbit skin resulted in moderate redness. This irritation may have been mechanical because the cotton patches under which the test material was applied adhered to the skin.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

26.04.2002 (30)

Species	:	rabbit
Concentration	:	other: undiluted 45% aqueous commercial material
Exposure	:	Open
Exposure time	:	10 day
Number of animals	:	1
PDII	:	
Result	:	not irritating
EC classification	:	not irritating
Method	:	other: Dow range-finding
Year	:	1980
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The skin irritation test included topical application of neat Dowfax 8390 to the inner surface of the left ear (0.1 ml) (open) and to intact and abraded skin on the abdomen (0.5 ml each) of 1 male New Zealand White rabbit. Ten daily applications were made to the ear and intact abdominal site and 3 to the abraded abdominal site. The rabbit was weighed on days 1, 7 14, and 23. It was evaluated daily on weekdays through day 14 and on day 23.
Result	:	Contact with this 45% aqueous XD 8390 material on unconfined rabbit skin resulted in no irritation.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

26.04.2002 (30)

Species	:	rabbit
Concentration	:	other: undiluted 45% commercial liquid used
Exposure	:	Occlusive
Exposure time	:	10 day
Number of animals	:	1
PDII	:	
Result	:	slightly irritating
EC classification	:	not irritating
Method	:	other: Dow range-finding
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The skin irritation test included topical application of neat Dowfax 8390 to the inner surface of the left ear (0.1 ml) (open) and to intact and abraded skin on the abdomen (0.5 ml each) of 1 male New Zealand White rabbit. Ten daily applications were made to the ear and intact abdominal site and 3 to the abraded abdominal site. The rabbit was weighed on days 1, 6, 15 and 18. It was evaluated daily on weekdays through day 11 and on days

15 and 18.

Result	:	Very slight to slight erythema and sporadic exfoliation from superficial burning was observed upon prolonged, repeated contact with intact or abraded abdominal skin.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

26.04.2002 (31)

Species	:	rabbit
Concentration	:	other: undiluted 45% commercial liquid
Exposure	:	Open
Exposure time	:	10 day
Number of animals	:	1
PDII	:	
Result	:	not irritating
EC classification	:	not irritating
Method	:	other: Dow range-finding
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The skin irritation test included topical application of neat Dowfax 8390 to the inner surface of the left ear (0.1 ml) (open) and to intact and abraded skin on the abdomen (0.5 ml each) of 1 male New Zealand White rabbit. Ten daily applications were made to the ear and intact abdominal site and 3 to the abraded abdominal site. The rabbit was weighed on days 1, 7 14, and 23. It was evaluated daily on weekdays through day 14 and on day 23.
Result	:	There was no irritation observed on the ear site at any time.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

26.04.2002 (31)

Species	:	rabbit
Concentration	:	other: undiluted commercial liquid
Exposure	:	Open
Exposure time	:	2 day
Number of animals	:	1
PDII	:	
Result	:	not irritating
EC classification	:	not irritating
Method	:	other: Dow range-finding
Year	:	1995
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The skin irritation test included topical application of neat Dowfax 8390 to the inner surface of the left ear (0.1 ml) (open) and to intact and abraded skin on the abdomen (0.5 ml each) of 1 male New Zealand White rabbit. Two applications were made and no more due to severe irritation.
Result	:	No irritation was observed at the ear application site.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (28)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	5 % active substance
Dose	:	.1 ml
Exposure Time	:	24 hour(s)
Comment	:	

Number of animals	:	6
Result	:	moderately irritating
EC classification	:	not irritating
Method	:	OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year	:	1998
GLP	:	yes
Test substance	:	other TS
Method	:	The eyes of 6 adult New Zealand white rabbits were examined with 2% aqueous fluorescein stain and established as being free of defects/irritation the day prior to study start. A 0.1 ml aliquot of the 5% aqueous Dowfax 8390 was instilled into the conjunctival sac of the right eye of 3 male and 3 female rabbits. The eyelid of each rabbit was held closed for approximately one second after dosing. The left eye remained untreated and served as a control. The eyes of all rabbits remained unwashed for 24 hrs after dosing. The behavior of each rabbit was observed immediately post treatment for indications of pain or discomfort. An ocular anesthetic was used for both eyes of each rabbit after discomfort was observed in the first rabbit. Both eyes of the rabbits were examined with a binocular loupe and a white halogen light at 1, 24, 48 and 72 hrs and also 7 days post-instillation for conjunctival redness and chemosis, discharge, corneal opacity and reddening of the iris. The study was completed 7 days post-treatment. Rabbits were weighed on the day of treatment and at study termination.
Result	:	Slight or moderate conjunctival redness, slight or moderate chemosis, and slight or moderate ocular discharge were present in the treated eyes of all rabbits one hour after dosing. Twenty-four hours after dosing, all rabbits had moderate conjunctival redness, all rabbits had slight or moderate chemosis, 5 rabbits had slight or moderate ocular discharge, 5 rabbits had opacity of the cornea, and 1 rabbit had reddening of the iris. Forty-eight hours after dosing, all rabbits had slight or moderate conjunctival redness, 4 rabbits had slight or moderate chemosis, 2 rabbits had slight ocular discharge, and 5 rabbits had corneal opacity. Seventy-two hours after dosing, 3 rabbits had slight or moderate conjunctival redness, 3 rabbits had slight chemosis, 1 rabbit had slight ocular discharge, and 4 rabbits had corneal opacity. The ocular lesions were resolved in all animals 7 days after instillation of the test material and the study was terminated.
Test substance	:	The test material was a 5% (5% active) aqueous solution of Dowfax 8390.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (37)

Species	:	rabbit
Concentration	:	100 % active substance
Dose	:	50 other: mg
Exposure Time	:	
Comment	:	not rinsed
Number of animals	:	1
Result	:	highly irritating
EC classification	:	irritating
Method	:	OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year	:	1991
GLP	:	yes
Test substance	:	other TS
Method	:	The eyes of 1 adult New Zealand white rabbit were examined with an ophthalmoscope and established as being free of defects/irritation the day prior to study start. A 0.1 ml (50 mg) amount of the solid Dowfax 8390 was instilled into the conjunctival sac of the right eye of the rabbit. The eyelid was held closed for approximately one second after dosing. The left eye remained untreated and served as a control. The eyes of the rabbit remained unwashed. The behavior of the rabbit was observed immediately post treatment for indications of pain or discomfort. Both eyes of the rabbit were examined at 1, 24, 48 and 72 hrs and also 7 and 14 days post-

instillation for conjunctival redness and chemosis, discharge, corneal opacity and reddening of the iris. The study was completed 14 days post-treatment. The rabbit was weighed at the start of the study.

No additional animals were tested due to the adverse reaction.

This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.

Result : A single application of the test material produced opalescent corneal opacity, iridial inflammation and severe conjunctival irritation. Other adverse ocular effects were vascularization of the cornea and pale areas over the nictitating membrane. The test material produced a maximum total score of 53 and was considered at least a severe irritant (Class 6 on a 1 to 8 scale) to the rabbit eye according to a modified Kay and Calandra classification system.
Test substance : The test material was the solid/powdered Dowfax 8390.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (38)

Species : rabbit
Concentration : other: undiluted commercial liquid product
Dose : .1 ml
Exposure Time :
Comment : not rinsed
Number of animals : 3
Result : moderately irritating
EC classification : not irritating
Method : Directive 84/449/EEC, B.5 "Acute toxicity (eye irritation)"
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : The eyes of 3 female New Zealand white rabbits were examined for defects the day prior to study start. A 0.1 ml aliquot of the aqueous Dowfax 8390 was instilled into the conjunctival sac of the left eye of each rabbit. The eyelid of each rabbit was held closed for approximately two seconds after dosing. The right eye remained untreated and served as a control. The behavior of each rabbit was observed immediately post treatment for indications of pain or discomfort. Both eyes of the rabbits were examined at 1, 24, 48 and 72 hrs and also 7, 14 and 21 days post-instillation for conjunctival redness and chemosis, discharge, corneal opacity and reddening of the iris. The study was completed 21 days post-treatment.

The study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.

Result : Instillation of Dowfax XD 8390 into the eyes of 3 adult female rabbits resulted in corneal epithelial erosion which healed within 7 days, as well as moderate conjunctival reddening after initial marked chemosis. Except for slight conjunctival redness persisting in one animal, the effects were reversible within 21 days.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (39)

Species : rabbit
Concentration : other: undiluted commercial liquid
Dose : .1 ml
Exposure Time :
Comment : other: one eye was washed after 30 seconds and the other after 1 hr
Number of animals : 1
Result : moderately irritating
EC classification :

Method	:	other: Dow range-finding
Year	:	1995
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	0.1 ml of neat Dowfax 8390 was instilled into each conjunctival sac of a female NZW rabbit. One eye was washed with water after 30 seconds, while the other eye was washed with water after one hr. The animal was evaluated immediately (for pain and other effects), at 1, 24, 48, and 72 hrs and 7, 14 and 21 days.
Result	:	The animal survived the test period and there were no clinical signs of systemic toxicity. Moderate discomfort was exhibited by the animal immediately after instillation of the test material in the first eye. Then, Ophthaine ocular anesthetic was instilled both eyes prior to dosing the second eye. Slight to moderate conjunctival redness and swelling was observed in both eyes from immediately after dosing through the 72 hr read. The 30-second exposure eye had very slight conjunctival response at the 7 and 14 day checks. The 30-second exposure eye had very slight irritation of the iris immediately after dosing through 72 hrs and the 1 hr eye had very slight irritation of the iris from 1 hr after dosing through 48 hrs. The 30-second eye had very slight to slight corneal opacity after staining with fluorescein, from the 1 hr read through the 14 day read. The hour eye had very slight corneal opacity after staining from 1 hr after dosing through 72 hrs. Ocular irritation was resolved in both eyes by 21 days and the study terminated.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (28)

Species	:	rabbit
Concentration	:	other: solid material as is
Dose	:	
Exposure Time	:	
Comment	:	other: one eye washed after 30 seconds the other after one hr
Number of animals	:	1
Result	:	moderately irritating
EC classification	:	
Method	:	other: Dow range-finding
Year	:	1987
GLP	:	no
Test substance	:	other TS
Method	:	0.1 g of neat XU-40341.00 Dowfax* 8390 was instilled into each conjunctival sac of a male NZW rabbit. One eye was washed with water after 30 seconds, while the other eye was washed with water after one hr. The animal was evaluated immediately (for pain and other effects), at 1, 24, 48, and 72 hrs and 7, and 14 days. Ophthalmic anesthetic was administered to alleviate discomfort experienced by the rabbit.
Result	:	A single exposure of NZW rabbit eyes to the test material resulted in moderate discomfort, moderate conjunctival redness and swelling, moderate reddening of the iris, and moderate corneal injury. Ocular effects, which included corneal injury, were absent at day 14 of the test in the eye washed at 30 seconds. The rabbit was inadvertently euthanized prior to day 21 so no further information was available.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (29)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure Time	:	

Comment	:	other: one eye washed after 30 seconds and the other after 1 hr
Number of animals	:	1
Result	:	moderately irritating
EC classification	:	
Method	:	other: Dow range-finding
Year	:	1980
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	0.1 ml of neat Dowfax 8390 was instilled into each conjunctival sac of a female NZW rabbit. One eye was washed with water after 30 seconds, while the other eye was washed with water after one hr. The animal was evaluated immediately (for pain and other effects), at 1, 24, 48, and 72 hrs and 7, and 14 days.
Result	:	Instillation of this material into the eyes of a rabbit resulted in slight discomfort, moderate conjunctival redness and swelling, moderate reddening of the iris, and moderate corneal injury. All signs of eye irritation were absent by 14 days post-exposure.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

26.04.2002 (30)

Species	:	rabbit
Concentration	:	other: undiluted 45% commercial liquid
Dose	:	.1 ml
Exposure Time	:	
Comment	:	other: one eye washed after 30 seconds and the other after 1 hr
Number of animals	:	1
Result	:	highly irritating
EC classification	:	
Method	:	other: Dow range-finding
Year	:	1974
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	0.1 ml of neat Dowfax 8390 was instilled into each conjunctival sac of a female NZW rabbit. One eye was washed with water after 30 seconds, while the other eye was washed with water after one hr. The animal was evaluated immediately (for pain and other effects), at 1, 24, 48, and 72 hrs and 7, and 14 days.
Result	:	Instillation of the undiluted 45% aqueous solution into the eyes of a rabbit resulted in pain, severe conjunctival inflammation, moderate iritis, and moderate corneal injury.
Reliability	:	(2) valid with restrictions
Flag	:	Material Safety Dataset

26.04.2002 (31)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	Induction .5 % intracutaneous Induction 50 % other: not stated Challenge 50 % occlusive epicutaneous
Number of animals	:	10
Vehicle	:	water
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	OECD Guide-line 406 "Skin Sensitization"
Year	:	1998
GLP	:	yes
Test substance	:	other TS

Method	:	The concentration of the test material used in the main study was based on the results of a pretest. Ten test and 5 control female Dunkin-Hartley guinea pigs were used for the main study. Intradermal induction consisted of two injections (0.1 ml per site) of the test material (0.5% w/v in water), with and without Freund's Complete Adjuvant, and a control with Adjuvant alone. After one week, the scapular area between the two intradermal injection sites (one day before the topcial treatment the skin was rubbed with 10% w/v) sodium dodecyl sulfate to increase sensitivity) was treated topically for 48 hours with 0.5 ml of a 50% (w/v) dilution of the test material in water. Induction readings were made at day 3 (after intradermal injection) and day 10 (after epidermal exposure). Challenge on day 22 consisted of a single, 24-hour, topical application (0.5 ml) of the test material at concentrations of 20 and 50% w/v in water on two separate sites on the right flank of each test and control animal under an occlusive dressing. Observations for any dermal reaction were made approximately 24 and 48 hrs after removal of the dressing. A rechallenge was conducted approximately one week after the first challenge with a 5 and 10% (w/v) of the test material. The study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.
Result	:	During the induction phase, severe erythema was noted at all intradermal injection sites treated with Adjuvant and test material including signs of necrosis with 3 animals. Well defined to moderate erythema was observed in most cases of the epidermally treated induction sites of the experimental animals. Between the controls and the experimental animals there was no significant difference noted at the challenge sites 24 and 48 hrs after removal fo the dressings with corresponding test material concentations of 5, 10, 20 and 50%.
Test substance	:	Test material was Dowfax* 8390-D, which is the powdered material. It was used as dilutions in water, as noted elsewhere.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint
26.04.2002		(40)

Type	:	Guinea pig maximization test
Species	:	guinea pig
Concentration	:	Induction .1 % intracutaneous Induction 5 % occlusive epicutaneous Challenge 2 % occlusive epicutaneous
Number of animals	:	20
Vehicle	:	water
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	Directive 84/449/EEC, B.6 "Acute toxicity (skin sensitization)"
Year	:	1991
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Concentrations of the test material were selected based on the results of sighting tests. Twenty test animals and ten control animals were used for the main study. Induction of the test animals was carried out with intradermal injections (0.1 ml) of (i) Freund's Complete adjuvant in distilled water, (ii) 0.1% active ingredient (w/v) in distilled water and (iii) 0.1% active ingredient (w/v) in a preparation of Freund's Complete Adjuvant plus distilled water. One week later, the same skin area was treated with a topical application of 0.2-0.3 ml of the test material (5% active ingredient v/v in distilled water) under an occlusive dressing which remained in place for 48 hrs. Control animals were treated with identical intradermal injections except without test material; also, the topical application for the controls consisted of the vehicle alone.

Test animals were challenged on day 21 with 0.1-0.2 ml of a 2% solution of Dowfax 8390 (v/v in distilled water) applied to the skin under occlusive dressing for 24 hrs. The vehicle alone was applied as a control. Dermal reactions were evaluated at 24 and 48 hrs after the dressings were removed.
One test animal died of undetermined causes.

Study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.

Result : Dowfax 8390 did not result in any skin sensitisation (0 of 19 animals) after induction with a solution which contained 5% active ingredient.
Test substance : Dowfax 8390 surfactant solution was submitted as the 35% aqueous solution. Application amounts are stated as percent of active ingredient.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (41)

Type : Buehler Test
Species : guinea pig
Concentration : Induction 75 % occlusive epicutaneous
Challenge 75 % occlusive epicutaneous

Number of animals : 20
Vehicle : water
Result : not sensitizing
Classification : not sensitizing
Method : Directive 84/449/EEC, B.6 "Acute toxicity (skin sensitization)"
Year : 1991
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : The study was also conducted in conformance with OECD Guideline Method B6, as well as Method 406.

The concentrations of the test material for the main study were based on preliminary topical studies. Twenty treated and 10 control Dunkin-Hartley guinea pigs were used for the main study. Induction consisted of 3 topical applications (0.5 ml) of 75% w/w concentration of the test material in distilled water (or distilled water alone for the controls) on days 0, 7 and 14. The 6-hour applications were on the same site under an occlusive dressing; the test sites were evaluated for any irritation response 24 hrs after each induction.

Challenge on day 28 consisted of a single, 6-hour, topical application (0.5 ml) of the test material at a concentration of 75% w/w in distilled water under occlusive dressing. Observations for any dermal reaction were made approximately 24 and 48 hrs after removal fo the patches.

This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.

Result : Induction with the test material did not produce any adverse reaction. Challenge with the test material did not result in a sensitization reaction in any of the treated animals. Thus, the test material was a non-sensitizer to the skin of guinea pigs.
Test substance : The test material was Dowfax 8390 surfactant, a 35% solution in water. Dosing concentrations were (w/w), implying that 75% is 75% of 35% active ingredient (i.e., not calculated based on active ingredient).
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (42)

Type : Buehler Test
Species : guinea pig

Concentration	:	Induction undiluted occlusive epicutaneous Induction 50 % occlusive epicutaneous Challenge 20 % occlusive epicutaneous
Number of animals	:	10
Vehicle	:	water
Result	:	sensitizing
Classification	:	sensitizing
Method	:	EPA OPP 81-6
Year	:	1991
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	This study was conducted in conformance with EPA guideline 81-6, but described as a modified Buehler method. Ten male Hartley albino guinea pigs received two dermal application of 0.4 ml of undiluted Dowfax 8390 during the 3 week induction period. All applications were made using 'Hill-Top Chambers'. The concentration of the test material used for the third induction application was decreased to 50% in distilled water due to erythema observed at the application site of two animals following the second induction application. Guinea pigs were challenged with 0.4 ml of 20% aqueous Dowfax 8390 two weeks after the last induction application. The concentrations of the test material used for the challenge application was decreased due to erythema observed at the application sites of 3 animals exposed to the test material following the third induction application. The condition of the test sites was assessed approximately 24 and 48 hours after the challenge application.
Result	:	Challenge application with 0.4 ml of Dowfax 8390 caused slight erythema at the test site in 9 of 10 animals. Therefore, under the conditions of this study, Dowfax 8390 has the potential to cause delayed contact hypersensitivity in guinea pigs.
Test substance	:	The Dowfax 8390 used in this study was 35% solids/active in water.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (43)

Type	:	Buehler Test
Species	:	guinea pig
Concentration	:	Induction 2.9 % occlusive epicutaneous Induction 1.5 % occlusive epicutaneous Challenge 1.5 % occlusive epicutaneous
Number of animals	:	10
Vehicle	:	water
Result	:	not sensitizing
Classification	:	not sensitizing
Method	:	other: none stated other than 'modified Buehler'
Year	:	1991
GLP	:	yes
Test substance	:	other TS
Method	:	A modified Buehler method was used. This method was the same as one described in Berdasco, 1991, in which the Data Requirement was 'Guideline Reference No. 81-6 --40 CFR Part 158.135'. Ten male Hartley albino guinea pigs received two dermal applications of 0.4 ml of 2.9% Dowfax 8390 in distilled water during the three week induction period. The concentration of the test material used for the third induction application was decreased to 1.5% due to erythema observed at the application site of one animal following the second induction application. Guinea pigs were challenged with 0.4 ml of 1.5% Dowfax 8390 two weeks after the last induction application. The condition of the test sites was assessed approximately 24 and 48 hours after the challenge application.
Result	:	Challenge application with o.4 ml of 1.5% Dowfax 8390 caused no

erythema or edema at the application site in any animal tested. Therefore, under the conditions of this study, 2.9% Dowfax 8390 does not cause delayed contact hypersensitivity in guinea pigs.

Test substance : The test material was a use dilution of Dowfax 8390 containing 2.9% (does not state 2.9% of what--active ingredient or 2.9% of normal 35% Dowfax 8390).
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (44)

Type : Buehler Test
Species : guinea pig
Concentration : Induction undiluted occlusive epicutaneous
Challenge undiluted occlusive epicutaneous

Number of animals : 20
Vehicle :
Result : sensitizing
Classification : sensitizing
Method : other: stated 'Buehler'
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : In this Buehler test, 20 female guinea pigs were exposed to 0.5 ml of undiluted test substance, by topical application to the same site on the scapula region during the induction phase. These induction applications were made on 9 separate occassions during a 3 week period; each induction exposure was for 6 hours duration using an occlusive patch.

Ten days after the last induction exposure, the animals were challenged by application of 0.5 ml of undiluted test substance to the contralateral flank. The challenge sites were then examined at 24, 48 and 72 hours after removal of dressings. A second challenge application was carried out three weeks after the first one.

This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.

Result : Evidence of a skin sensitization reaction was observed for 14 animals after the first challenge, and for 9 animals after the second challenge. It was concluded that the test substance induced delayed contact hypersensitivity in the guinea pig.
Test substance : The test material was Dowfax* XD 8390, used undiluted.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (45)

5.4 REPEATED DOSE TOXICITY

Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : 90 days
Frequency of treatment : continuous
Post obs. period : None
Doses : 0, 50, 100, 200 or 600 mg/kg/day
Control group : yes
NOAEL : = 100 mg/kg
LOAEL : = 200 mg/kg

Method	:	other: Dow historic
Year	:	1976
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of 15 Sprague-Dawley rats/sex/dose were maintained for 90-91 days on diets containing sufficient Dowfax surfactant XD-8390 to provide doses of 0, 50, 100, 200 or 600 mg/kg/day to assess the toxicological effects that might be associated with daily ingestion by rats for 90 days. Doses were chosen on the basis of a 2-week tolerance study. Liver and kidney 'injury' was observed at doses of 1000 mg/kg/day and higher but no discernible changes in appearance, demeanor or gross examination of tissues and organs were observed at 300 mg/kg/day. Parameters examined were weekly body weights, twice weekly clinical observations, hematology (RBC, WBC & diff, PCV, Hgb) on 10 rats/sex of control and high dose during the final week of study, urinalysis on 10 rats/sex/dose on last day of study (pH, sp. gr., glucose, ketones, bilirubin, occult blood, protein, specific gravity), clinical chemistry (UN, AP, SGOT, SGPT) on all rats in last week of study, complete gross exam of all rats at necropsy, organ weights (brain, heart, liver, kidneys and testes), microscopic examination of a broad range of tissues from all ten rats/sex of the control and high dose. Similar sections of liver and kidney were also prepared from 10 rats/sex of the group receiving 200 mg/kg/day. Also the livers from 4-5 rats/sex of the high dose and control were cut on a freezing microtome and stained with Oil Red O to evaluate lipid content. The eyes of 10 rats/sex/dose were examined at necropsy and also histologically.
Result	:	Morphological manifestations which could be associated with ingestion of the test material were observed only at the two higher dose levels, 200 and 600 mg/kg/day and were limited to effects on the kidneys. The weights of the kidneys were significantly increased at the two higher dose levels among the females and at the highest dose level among the males. The kidneys of these groups of rats appeared swollen at the time of necropsy and among the females, a slight dilatation in the renal tubules was observed microscopically at the highest dose level. The kidney morphology and function was not different from that of control rats at the two lower dose levels. The SGPT activity was increased at all dose levels in the male rats in the absence of any histological or other biochemical evidence of liver change. Except for these changes no alterations in other parameters were observed at any dose level.
Test substance	:	The test material submitted was XD-8390, composed of 37.6% active ingredient. Attempts to incorporate the formulated liquid into the ground laboratory chow were unsatisfactory; thus, the solution of XD-8390 was dried to a fine powder for incorporation in the diets. The dry powder was kept in air-tight containers until used because of its hygroscopic nature. So, the doses were based on amount of active ingredient.This was a different lot than that used in the 90-day dog study.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (46)

Species	:	rat
Sex	:	male/female
Strain	:	other: CD, remote Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	28 days
Frequency of treatment	:	daily
Post obs. period	:	None
Doses	:	50, 250, 1000 mg active ingredient/kg body weight/day

Control group	:	yes, concurrent vehicle
NOAEL	:	= 250 mg/kg
LOAEL	:	= 1000 mg/kg
Method	:	other: none particularly specified
Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Male and female CD rats were given Dowfax XD 8390 (primarily C-16 alkylated sodium sulfonated diphenyl oxide) by oral gavage at doseage levels of 0, 50, 250 or 1000 mg/kg/day for 28 consecutive days. Doses were not checked analytically. Necropsy of all surviving animals was performed on day 29. Observations included 3x daily clinical observations, weekly food consumption, visual water consumption, 2x weekly body weights, weekly food conversion calculations, hematology (PCV, Hb, RBC, WBC, platelets, WBC diff, MCHC, MCV, MCH) on day 25, clinical chemistries (AP, ALT, AST, BUN, creatinine, glucose, total bilirubin, total protein, electrophoretic protein fraction, Na, K) on day 25, urinalysis (appearance, volume, pH, sp.gr., protein, total reducing substances, glucose, ketones, bilirubin, urobilin, nitrite, blood, sed.) on day 21, macroscopic pathology of all animals, organ weights (adrenals, heart, kidneys, liver, spleen, testes), histopathology of all rats (adrenals, heart, kidneys, liver, spleen, stomach). Appropriate statistical methods were used.
Result	:	There were no differences in the food consumption of control and treated animals, but body weight gains and food utilization efficiency of male rats in the 1000 mg/kg/day group were lower than for controls. Post-dosing salivation and loose feces were observed throughout the study in the 1000 mg/kg/day group. There were changes in several clinical chemistry parameters for rats in the 1000 mg/kg/day group, and at necropsy the absolute and relative liver and kidney weights of high dose females were higher than for controls. There were no internal macroscopic changes observed at necropsy which were related to treatment, but histopathologic examinations revealed microscopic changes in the livers of some of the animals in the 1000 mg/kg/day group. There were no adverse treatment-related effects in either male or female rats in the 250 mg/kg/day or 50 mg/kg/day groups.
Test substance	:	The test material was XD 8390, a brown liquid with 36.7% active ingredient. The doses were mg active ingredient.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (47)

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Crj: CD(SD)
Route of admin.	:	gavage
Exposure period	:	47 days for males and 50-54 days for females
Frequency of treatm.	:	daily
Post exposure period	:	
Doses	:	25, 75 and 250 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL	:	= 25 mg/kg bw
LOAEL	:	= 75 mg/kg bw
Method	:	other: OECD 422
Year	:	
GLP	:	yes
Test substance	:	
Method	:	Groups of 12 male and 12 female CD rats were administered the test

material 7 days/week by gavage at dose levels of 0 (control), 25, 75, or 250 mg/kg/day. These dose levels represented doses of the actual surfactant present at 37% in the aqueous sample. The females were dosed once daily for 2 weeks prior to breeding, continuing through breeding (2 weeks), gestation (3 weeks), lactation (4 days) and until the day of necropsy (test day 50 or 54). Females exhibiting active signs of parturition at the time of scheduled gavage were not dosed on that particular day (comment was made on dosing record). The males were dosed once daily for 2 weeks prior to breeding and continuing through breeding (2 weeks) up until the day of necropsy (test day 47). Effects on general toxicity, neurobehavioral activity as measured by sensory evaluation, rectal temperature, forelimb and hindlimb grip strength and motor activity, clinical pathology, gonadal function, mating behavior, conception, development of the conceptus, parturition and early postnatal growth, and survival, were evaluated. Clinical pathology included hematology (hematocrit, hemoglobin concentration, platelet cell, red blood cell, total white blood cell and differential white blood cell counts and prothrombin time), clinical chemistry (alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase activities, albumin, cholesterol, creatinine, electrolytes (Na, K, PO4, Cl and Ca), glucose and total bilirubin) and urinalysis (pH, bilirubin, glucose, proteins, ketones, blood, urobilinogen, total protein and urea nitrogen). In addition, a gross necropsy of the adults was conducted with extensive histopathologic examination of tissues. In the offspring, litter size, pup survival, sex, body weight, and the presence of gross external abnormalities were assessed.

Result : Mortality: One male from the 25 mg/kg/day group and two females from the 75 mg/kg/day group died during the course of the study. The male died on test day 16 while the females died on gestation day 15 and lactation day 5. In each instance the cause of death appeared to be due to a gavage dosing error.

Clinical Observations: The only clinical observation considered to be treatment related consisted of increased incidences of respiratory difficulties at all dose levels which was most likely related to aspiration of small amounts of surfactant test material. At the lowest dose level, 25 mg/kg/day, respiratory difficulty was observed in only one male rat. Other clinical observations which were not considered to be treatment related included clear perioral soiling (both sexes), clear perinasal soiling (males only), red perinasal soiling (males only) and decreased/soft feces. These clinical observations were not considered to be treatment related because they were observed sporatically. Most animals were only observed with red perinasal soiling once during the study. The highest incidence of this finding in one animal was four.

Body weight and feed consumption of male and female rats gavaged with Dowfax 8390 were comparable to control values. Reproductive indices, pup survival and sex ratio data of pups of male and female rats gavaged with Dowfax 8390 were comparable to control values. There were no visible external morphologic alterations noted in any of the offspring.

Functional tests: There was no effect on functional tests, including sensory evaluation, hindlimb and forelimb grip performance and motor activity.

Clinical Pathology: Prothrombin times of male rats gavaged with 75 (19% increase) or 250 (35% increase) mg/kg/day were statistically significantly increased from control male values (Table 1). The increase in prothrombin time had no apparent functional impact as evidenced by the lack of any unusual bleeding in males. Prothrombin times of female rats gavaged with 250 mg/kg/day were statistically significantly decreased from control values. This was considered to be spurious as it was not consistent with the effect noted in males and similar increases in prothrombin time were not seen in females administered higher doses in the initial phase of the

study.

There were no treatment-related hematologic effects at any dose level.

Males and females gavaged with 250 mg/kg/day had statistically significant increases in mean alanine transaminase (ALT) activity (Table 2). Statistically significant increase in the mean aspartate transaminase (AST) activity was also seen in females given 250 mg/kg/day (Table 3). Although AST activity for the high dose females was within the historical control range, it was interpreted to be treatment-related due to a concomitant increase in serum ALT levels. An increase in these 'leakage' enzymes, particularly ALT, is usually indicative of hepatocellular injury. In this case, there was no significant histologic evidence of hepatocellular injury.

A slight but statistically significant decrease in total serum protein was noted in males gavaged with 250 mg/kg/day (Table 2). This minimal decrease was within the historical control range and interpreted to be not treatment-related.

Males gavaged with 250 mg/kg/day had slightly lower urine volume and slightly higher specific gravity relative to controls (Table 4). The lower urinary volume and higher specific gravity were within the historical control range and thus interpreted as not treatment-related.

Urine samples from males gavaged with 25 mg/kg/day or greater showed a higher incidence of alkalinuria with a urinary pH of 8.5 or 9 for most of the animals. In the absence of any significant serum electrolyte alterations and lack of evidence of histological changes in the kidneys, the higher incidence of alkalinuria may be due to the urinary excretion of the test material and/or it's metabolites.

Five of twelve males gavaged with 250 mg/kg/day had bilirubinuria (1+) as compared to one out of twelve controls. This increase in the incidence of bilirubinuria in this treatment group was interpreted to be secondary to the increase of urine specific gravity. All five rats with 1+ bilirubinuria had a urine specific gravity of 1.064 or above compared to the control mean of 1.046. Secondly an increased incidence of 1+ bilirubinuria has also been noted in historical controls and therefore this change was interpreted to be not treatment-related.

Two of twelve males gavaged with 250 mg/kg/day had blood (4+) in the urine. The reason for the hematuria in these two animals was not apparent as their individual prothrombin times (13.6 and 13.9 seconds, respectively) were within the range of the concurrent controls (11.6 - 14.5 seconds) and there were no gross or histological indications of hemorrhage, inflammation, or trauma in the urinary tract examined.

Anatomic pathology: There were no treatment-related differences in any of the organ weights for male or females at any dose level.

Gross pathology: Three animals died spontaneously during the course of the study. In each case the lesions were consistent with inadvertent gavage complications which was the cause of death.

Gross observations in the lungs such as, generalized edema, pale/dark focus, froth and mottled lungs were consistent with gavage complications observed at scheduled necropsy.

Histopathologic observations: There were no treatment-related histopathological changes attributed to the direct systemic toxicity of Dowfax 8390.

The lungs and trachea of some animals of both sexes gavaged with 25, 75 or 250 mg/kg/day had histopathologic changes consistent with aspiration into the respiratory tract following reflux of the test material (possibly due to the surfactant properties of the test material) that may have occurred during the course of repeated oral gavage and/or inadvertent gavage errors (Table 5). These changes consisted of very slight, slight or moderate, multifocal, chronic/chronic-active inflammation of the bronchi, bronchioles and the alveoli. Very slight to slight perivascular eosinophilic inflammation was seen in the lungs of some males and females, with or without inflammatory changes in the airways. The perivascular eosinophilic inflammatory response was interpreted to be a part of the inflammatory reaction triggered by the inadvertent entry of Dowfax 8390 into the respiratory tract during the process of repeated oral gavage. A very slight degree of perivascular eosinophilic inflammation was, however, seen in one control female, the reason for which was not apparent. All these changes were random in distribution and did not involve all of the lung lobes.

Test substance : Disodium hexadecyldiphenyloxide disulfonate and disodium dihexadecyldiphenyloxide disulfonate constituted 36.7 ± 0.06% of the sample. The test material also contained small amounts of sodium sulfate (1.5% maximum) and sodium chloride (< 1%) with the balance comprised of water. Infrared spectroscopy was used to confirm the proposed structure of Dowfax 8390 surfactant.

Attached document :

Text Table 1. Prothrombin Time – Statistically Identified Differences

Parameter	Historical Control Data: Study 1[a]	0 MKD	25 MKD	75 MKD	250 MKD
Prothrombin Time(males)	12.1	12.4	13.2	**14.8***	**16.7***
Prothrombin Time (female)	11.8	12.0	12.0	11.7	11.3*

[a] Inhalation study conducted in 2003
* Statistically different from control mean (alpha = 0.05).
Bold type indicates treatment related effect.
time = seconds

Text Table 2. Clinical Chemistry – Statistically Identified Differences (Males)

Parameter	Historical Control Data: Study 1[a]	Study 2[a]	Study 3[b]	0 MKD	25 MKD	75 MKD	250 M
Urea Nitrogen (mg/dl)	15	13	14	17	16	14*	15
ALT (u/l)	29	33	32	47	40	40	**83**
Total Protein (g/dl)	6.4	6.3	6.2	6.6	6.5	6.4	6.3

[a] Inhalation studies
[b] Oral gavage study (The two inhalation studies and the one oral gavage study were done since 2000)
* Statistically different from control mean (alpha = 0.05)
Bold type indicates treatment-related effect.

Text Table 3. Clinical Chemistry – Statistically Identified Differences (Females)

Parameter	Historical Control Data			0 MKD	25 MKD	75 MKD	250 MKD
	Study 1[a]	Study 2[a]	Study 3[b]				
ALT (u/l)	36	63	27	30	31	33	**69***
AST (u/l)	94	120	107	77	76	78	**96***

[a] Inhalation studies
[b] Oral gavage study (The two inhalation studies and the one oral gavage study were done since 2000)
* Statistically different from control mean (alpha = 0.05)
Bold type indicates treatment-related effect.

Text Table 4. Urinalysis (Males)

Parameter	Historical Control Data		0 MKD	25 MKD	75 MKD	250 MKD
	Study 1[a]	Study 2[b]				
Volume (ml)	7.2	9.7	14.3	14.1	13.1	10.3
Specific Gravity	1.067	1.057	1.046	1.043	1.049	1.059
pH	7.0 (3) 7.5 (4) 8.0 (2) 8.5 (3)	7.0 (1) 7.5 (3) 8.0 (1) 8.5 (3) ≥ 9 (3)	7.0 (1) 7.5 (1) 8.0 (7) 8.5 (3)	8.0 (2) **8.5 (6)** **≥ 9 (3)**	**8.5 (10)** **≥ 9 (2)**	7.5 (1) 8.0 (1) 8.5 (1) **≥ 9 (9)**
Bilirubin	Neg (7) + (5)	Neg (9) + (2)	Neg (11) + (1)	Neg (10) + (1)	Neg (11) + (1)	Neg (7) + (5)
Blood	Neg (10) + (2)	Neg (10) + (1)	Neg (11) + (1)	Neg (11)	Neg (12)	Neg (10) ++++ (2)

[a] Inhalation study
[b] Oral gavage study (The inhalation and the oral gavage studies were done since 2000)
Bold type indicates treatment-related effect.

Text Table 5. Gavage Induced Lesions of the Lungs and Trachea

Sex	Males				Females			
Dose (MKD)	0	25	75	250	0	25	75	250
Number Examined	12	12	12	12	12	12	12	12
Lung Inflammation; chronic; bronchi-bronchiole; bronchiolo-alveolar; multifocal *Very slight*	0	0	0	0	0	0	0	1
Slight	0	0	1	0	0	0	0	1
Moderate	0	0	0	2	0	0	0	0
Inflammation; chronic active; bronchi-bronchiole; bronchiolo-alveolar; multifocal *Very slight*	0	0	0	1	0	0	0	0
Slight	0	0	1	0	0	0	0	1
Moderate	0	0	1	0	0	0	0	0
Inflammation; eosinophilic; perivascular; multifocal *Very slight*	0	2	1	1	1	1	0	1
Slight	0	0	1	1	0	0	1	1
Inflammation; chronic; pleura; focal *Slight*	0	0	0	1	0	0	0	0
Trachea Hyperplasia;regenerative, epithelium; diffuse *Very slight*	0	0	1	0	0	0	0	0
Slight	0	0	1	1	0	0	0	0
Inflammation; subacute to chronic; lamina propria; submucosa; focal *Slight*	0	0	0	0	0	0	0	1

Conclusion : The No-Observable-Adverse-Effect Level (NOAEL) for general toxicity was 25 mg/kg/day, while 250 mg/kg/day was a no-observable-effect level (NOEL) for reproductive and neurological effects. Gavage administration of 250 mg/kg/day of Dowfax 8390 resulted in increased incidences of soft/decreased feces (males only), accompanied by slightly increased prothrombin times (males only), increased serum ALT (both sexes) and increased serum AST (females only) levels. At 75 mg/kg/day, prothrombin times were increased in males only. No toxicologically significant effects occurred in the 25 mg/kg/day group. Various respiratory symptoms were considered the result of gavage related aspirations of the surfactant test material. Urinalysis (conducted in males only) revealed a slight increase in urine pH at all dose levels thought to be associated with the properties of the test material and/or its metabolites, but with no toxicological sequelae.

Remark : The increase in prothrombin time is most likely due to the structural similarity between C16 Dowfax and Vitamin K or a precursor. In each case the side chain is of the same length. Similar effects were not observed with the C6 containing Dowfax and would not be expected with C10 or C12 containing Dowfax materials.

Reliability : (1) valid without restriction
1a: GLP guideline study

24.05.2006 (48)

Species : dog
Sex : male/female
Strain : Beagle

Route of admin.	:	oral feed
Exposure period	:	90-days
Frequency of treatment	:	continuous
Post obs. period	:	None
Doses	:	0, 50, 100 or 200 mg/kg/day
Control group	:	yes
NOAEL	:	= 200 mg/kg
Method	:	other: historic Dow method
Year	:	1976
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Male and female beagle dogs (4/sex/dose) were maintained for 90 days on diets containing sufficient Dowfax surfactant XD-8390 to provide doses of 0, 50, 100 or 200 mg/kg/day to assess the toxicological effects that might be associated with daily ingestion of this material by dogs for 90 days. Doses for this study were chosen subsequent to a tolerance study using doses of 250, 450 and 650 mg/kg. The lowest dose (250 mg/kg) caused a decrease in food consumption and approximately 5% loss in body weight--with greater decreases at the higher doses. Parameters examined were body weights weekly for the first month and then every 2 weeks, twice weekly food consumption/pen, daily clinical observations, hematology (RBC, WBC & diff, PCV, Hgb) prior to start of study and at 30, 84 and 90 days, urinalysis (pH, glucose, ketones, bilirubin, occult blood, protein, specific gravity and sed) on all dogs prior to study start and in last week of study, clinical chemistry (UN, AP, SGOT, SGPT) on all dogs prior to start of study and in last week of study, complete gross exam of all dogs at necropsy, organ weights (brain, heart, liver, kidneys and testes), microscopic examination of a broad range of tissues from all dogs in control and high dose, microscopic examination of kidneys from low and middle dose dogs, microscopic examination of additional sections of kidney from all dogs from all doses, and ophthalmologic examination of all dogs prior to study start and again prior to termination of the study. Also the livers from all high dose and control dogs were cut on a freezing microtome and stained with Oil Red O to evaluate lipid content.
Result	:	Effects which could be related to ingestion of the test material in the diet were limited to male and female dogs at the high dose level of test material, 200 mg/kg/day. Among these dogs, the weights of the kidneys and liver were slightly higher than that of control dogs. The difference was not statistically significant and there was no evidence of histological alterations among these organs in these dogs. No other parameters were significantly affected among dogs of either sex at any dose level of test material. Therefore, changes of toxicological significance which could be associated with ingestion of Dowfax surfactant XD-8390 were not observed in male or female beagle dogs at any dose level in this study.
Test substance	:	XD-8390 was submitted for this test. It was characterized as being 37.6% active material in water. Attempts to incorporate the formulated liquid into the ground laboratory chow were unsatisfactory; thus, the solution of XD-8390 was dried to a fine powder for incorporation in the diets. The dry powder was kept in air-tight containers until used because of its hygroscopic nature. So, the doses were based on amount of active ingredient.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (49)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test

System of testing	:	Salmonella typhimurium strains TA1535, TA1537, TA1538 TA98 and TA100
Concentration	:	10-500 micrograms/plate
Cycotoxic conc.	:	500 micrograms/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Eleven serial dilutions of the test substance, in approximately half-log steps, were plated with an appropriately diluted TA100 culture (equal numbers of bacterial cells/plate) onto non-selective agar. The percent survival of the TA100 culture was determined by comparing the number of colonies on the solvent control plate with those on the plates containing the test substance. The survival of strain TA100 was reduced at test substance concentrations from 100 micrograms/plate upwards and was eliminated at test substance concentrations from 3330 micrograms/plate upwards. Based on these data, the test substance was tested up to a concentration of 500 micrograms/plate. This study was conducted at the request of Dow Chemical Europe, Horgen, Switzerland.
Result	:	In the first two experiments with some strains several plates were infected with other bacteria. Thus, these parts of the test were repeated. All bacterial strains showed negative responses over the entire dose range of the test substance, i.e., no statistically significant dose-related increase in the number of revertants in two independently repeated experiments. The negative and strain-specific positive control values fell within the lab's historical ranges indicating that the test conditions were optimal and that the metabolic activation system functioned properly. Based on these results, the test substance was considered as nonmutagenic in the Ames Salmonella/microsome assay.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.04.2002 (50)

Type	:	Cytogenetic assay
System of testing	:	Cultured Peripheral Human Lymphocytes
Concentration	:	100, 333, 1000 and 3330 micrograms/ml
Cycotoxic conc.	:	1000 micrograms/ml (in absence of S-9) and 3330 micrograms/ml (presence of S-9)
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 473 "Genetic Toxicology: In vitro Mammalian Cytogenetic Test"
Year	:	1987
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The test was carried out in duplicate. Aroclor-1254 induced rat liver S9-mix was used as the metabolic activation system. Based on a dose selection study, the following doses were used in the main study: Without S-9: 100, 333, 1000 micrograms/ml Positive control MMC-C: 0.1 micrograms/ml With S-9: 333, 1000 and 3330 micrograms/ml Positive control CP: 20 micrograms/ml
Result	:	There were no statistically significant increases in the numbers of

chromosome aberrations at any of the concentrations tested, either in the presence or the absence of the metabolic activation system. Positive control chemicals, mitomycin C and cyclophosphamide, both produced a statistically significant increase in the incidence of chromosome aberrations.

It was concluded that the test substance was no clastogenic in human lymphocytes under the conditions of the assay.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
26.04.2002 (51)

Type : Cytogenetic assay
System of testing : Rat lymphocytes
Concentration : 0, 16.7, 50, 75, 100, 150, and 166.7 micrograms/ml of culture medium
Cycotoxic conc. : 500 micrograms/ml
Metabolic activation : with and without
Result : negative
Method : other: UK EMS (1990); OECD (Final Draft, 1997); EEC (1992); US EPA (1990)
Year : 1998
GLP : yes
Test substance : other TS
Method : Approximately 48 h after the initiation of whole blood cultures, cells in the absence and presence of rat liver S-9 activation were treated for 4 h with concentrations ranging from 0 (negative control), 50, 166.7, 500, 1000, 1667, 2500 and 5000 micrograms Dowfax 8390D Surfactant per ml of culture medium. The treated cultures were harvested approximately 20 h after the termination of the treatments. Mitotic indices data from this experiment indicated excessive toxicity at dose levels of 500 micrograms/ml. Hence, the experiment was repeated using dose levels of 1.7, 5, 16.7, 50, 100, 166.7, 500 and 1000 micrograms/ml. Based upon the mitotic indices, cultures treated with concentrations of 0, 50, 100 and 166.7 micrograms/ml in the absence of S-9 activation and cultures treated with targeted doses of 0, 16.7, 50 and 100 micrograms/ml in the presence of S-9 activation were selected for determining the incidence of chromosomal aberrations.

In a confirmatory assay with S-9, rat lymphocytes were treated as described above and harvested at 20 h and 44 h after treatment termination. In the absence of S-9, the treatment time was increased to 24 h and the treated cultures were harvested either at the end of the treatments or 24 h later. The incidence of chromosomal abnormalities was determined from cultures treated with 0, 25, 50 and 100 micrograms/ml in the absence of S-9 at the first harvest time, and from cultures treated with 0 and 150 micrograms/ml at the second harvest. In the presence of S-9, cultures treated with 0, 16.7, 50 and 75 micrograms/ml were used for evaluation at the first harvest and 0 and 150 micrograms/ml at the second harvest.

Result : In both assays, initial and confirmatory, there was no significant increase in the incidence of aberrant cells noticed at any of the treatment levels when compared to the corresponding negative control values.

Significant increases in the frequency of cells with aberrations were observed in cultures treated with the positive control chemicals, 0.075 micrograms/ml of MMC (without S-9) and 6 micrograms/ml of CP (with S-9).

Test substance : The test material was Dowfax* 8390-D which is the powdered form of the product. It is 97.5% active ingredient.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
26.04.2002 (52)

Type	:	HGPRT assay
System of testing	:	Chinese Hamster Ovary
Concentration	:	2.5 to 300 micrograms/ml
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 476 "Genetic Toxicology: In vitro Mammalian Cell Gene Mutation Tests"
Year	:	2001
GLP	:	yes
Test substance	:	other TS
Method	:	The genotoxic potential of the test material was assessed in two independent assays in the absence and presence of an externally supplied metabolic activation (S-9) system with concentrations ranging from 2.5 to 300 micrograms/ml. The adequacy of the experimental conditions for detection of induced mutation was confirmed by employing positive control chemicals, ethyl methanesulfonate for assays without S-9 and 20-methylcholanthrene for assays with S-9. Negative control cultures were treated with the solvent used to dissolve the test material.
Result	:	Dowfax 8390-D exhibited a steep dose response for cytotoxicity with an apparent threshold separating total cytotoxicity and compatibility with cell survival--a phenomenon typical to a number of detergents and surfactants. Because of this, the test material could be evaluated for mutagenicity only at non-cytotoxic concentrations. Based upon the frequency of TGr mutants recovered in cultures treated with the test material, it was concluded that Dowfax 8390-D surfactant did not induce a mutagenic response in the assay system employed.
Test substance	:	The test material was the dry powder version of Dowfax* 8390, called Dowfax* 8390-D. It is 98% active ingredient.
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

26.04.2002 (53)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Cytogenetic assay
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	90 days
Doses	:	0, 50, 100, 200 or 600 mg/kg/day
Result	:	negative
Method	:	other: scoring according to WHO, Buckton and Evans, 1973
Year	:	1977
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Five groups of 5 Sprague-Dawley (Spartan substrain) rats/sex were fed diets containing amounts of XD-8390 calculated to provide doses of 0, 50, 100, 200 or 600 mg/kg body weight per day for 90 days. Afte the 90-day treatment, bone marrow cells from all the rats were processed to capture cells in metaphase and plate them on glass slides. The chromosome analysis was similar to that described in WHO, Buckton and Evans, 1973. The slides were coded for blind scoring. The plan was to score 50 metaphase spreads per animal and only diploid (2n=42) or 2n-1 cells were scored.
Result	:	Analysis of 50 metaphase spreads from each of the 25 male rats revealed no chromosomal aberrations among the 1250 cells examined. Analysis of

1244 spreads from the 25 female rats revealed only one aberration (a chromatid break) in one animal at the 100 mg/kg dose level.

Although this abnormality was found in a treated animal, it was judged as 'probably inconsequential' because in similar studies with this strain of rats, 27 of 3750 cells (0.72%) from 100 untreated control rats contained one or more abnormalities. When this strain of rats was treated with a potent mutagen (triethylenemelamine), 55% of the bone marrow cells contained abnormal chromosomes.

Test substance : The test substance was submitted as a 36% aqueous solution. This was then dried to a 'fine hydroscopic powder' which contained 92.5% active ingredient. Test doses are based on this active ingredient.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

26.04.2002 (54)

5.7 CARCINOGENITY

5.8.1 TOXICITY TO FERTILITY

Type	:	other: OECD 422
Species	:	rat
Sex	:	male/female
Strain	:	Crj: CD(SD)
Route of admin.	:	gavage
Exposure period	:	47 days for males and 50-54 days for females
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	14 days
Female	:	14 days
Duration of test	:	
No. of generation studies	:	
Doses	:	25, 75 and 250 mg/kg/day
Control group	:	yes, concurrent vehicle
NOAEL parental	:	= 250 mg/kg bw
NOAEL F1 offspring	:	= 250 - mg/kg bw
Method	:	OECD Guide-line 422
Year	:	1996
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : Groups of 12 male and 12 female CD rats were administered the test material 7 days/week by gavage at dose levels of 0 (control), 25, 75, or 250 mg/kg/day. These dose levels represented doses of the actual surfactant present at 37% in the aqueous sample. The females were dosed once daily for 2 weeks prior to breeding, continuing through breeding (2 weeks), gestation (3 weeks), lactation (4 days) and until the day of necropsy (test day 50 or 54). Females exhibiting active signs of parturition at the time of scheduled gavage were not dosed on that particular day (comment was made on dosing record). The males were dosed once daily for 2 weeks prior to breeding and continuing through breeding (2 weeks) up until the day of necropsy (test day 47). Effects on general toxicity, neurobehavioral activity as measured by sensory evaluation, rectal temperature, forelimb and hindlimb grip strength and motor activity, clinical pathology, gonadal function, mating behavior, conception, development of the conceptus, parturition and early postnatal growth, and survival, were evaluated. Clinical pathology included

hematology (hematocrit, hemoglobin concentration, platelet cell, red blood cell, total white blood cell and differential white blood cell counts and prothrombin time), clinical chemistry (alkaline phosphatase, alanine aminotransferase and
aspartate aminotransferase activities, albumin, cholesterol, creatinine, electrolytes (Na, K, PO4, Cl and Ca), glucose and total bilirubin) and urinalysis (pH, bilirubin, glucose, proteins, ketones, blood, urobilinogen, total protein and urea nitrogen). In addition, a gross necropsy of the adults was conducted with extensive histopathologic examination of tissues. In the offspring, litter size, pup survival, sex, body weight, and the presence of gross external abnormalities were assessed.

Result : Mortality: One male from the 25 mg/kg/day group and two females from the 75 mg/kg/day group died during the course of the study. The male died on test day 16 while the females died on gestation day 15 and lactation day 5. In each instance the cause of death appeared to be due to a gavage dosing error.

Clinical Observations: The only clinical observation considered to be treatment related consisted of increased incidences of respiratory difficulties at all dose levels which was most likely related to aspiration of small amounts of surfactant test material. At the lowest dose level, 25 mg/kg/day, respiratory difficulty was observed in only one male rat. Other clinical observations which were not considered to be treatment related included clear perioral soiling (both sexes), clear perinasal soiling (males only), red perinasal soiling (males only) and decreased/soft feces. These clinical observations were not considered to be treatment related because they were observed sporatically. Most animals were only observed with red perinasal soiling once during the study. The highest incidence of this finding in one animal was four.

Body weight and feed consumption of male and female rats gavaged with Dowfax 8390 were comparable to control values. Reproductive indices, pup survival and sex ratio data of pups of male and female rats gavaged with Dowfax 8390 were comparable to control values. There were no visible external morphologic alterations noted in any of the offspring.

Functional tests: There was no effect on functional tests, including sensory evaluation, hindlimb and forelimb grip performance and motor activity.

Clinical Pathology: Prothrombin times of male rats gavaged with 75 (19% increase) or 250 (35% increase) mg/kg/day were statistically significantly increased from control male values (Table 1). The increase in prothrombin time had no apparent functional impact as evidenced by the lack of any unusual bleeding in males. Prothrombin times of female rats gavaged with 250 mg/kg/day were statistically significantly decreased from control values. This was considered to be spurious as it was not consistent with the effect noted in males and similar increases in prothrombin time were not seen in females administered higher doses in the initial phase of the study.

There were no treatment-related hematologic effects at any dose level.

Males and females gavaged with 250 mg/kg/day had statistically significant increases in mean alanine transaminase (ALT) activity (Table 2). Statistically significant increase in the mean aspartate transaminase (AST) activity was also seen in females given 250 mg/kg/day (Table 3). Although AST activity for the high dose females was within the historical control range, it was interpreted to be treatment-related due to a concomitant increase in serum ALT levels. An increase in these 'leakage' enzymes, particularly ALT, is usually indicative of hepatocellular injury. In this case, there was no significant histologic evidence of hepatocellular injury.

A slight but statistically significant decrease in total serum protein was noted in males gavaged with 250 mg/kg/day (Table 2). This minimal decrease was within the historical control range and interpreted to be not treatment-related.

Males gavaged with 250 mg/kg/day had slightly lower urine volume and slightly higher specific gravity relative to controls (Table 4). The lower urinary volume and higher specific gravity were within the historical control range and thus interpreted as not treatment-related.

Urine samples from males gavaged with 25 mg/kg/day or greater showed a higher incidence of alkalinuria with a urinary pH of 8.5 or 9 for most of the animals. In the absence of any significant serum electrolyte alterations and lack of evidence of histological changes in the kidneys, the higher incidence of alkalinuria may be due to the urinary excretion of the test material and/or it's metabolites.

Five of twelve males gavaged with 250 mg/kg/day had bilirubinuria (1+) as compared to one out of twelve controls. This increase in the incidence of bilirubinuria in this treatment group was interpreted to be secondary to the increase of urine specific gravity. All five rats with 1+ bilirubinuria had a urine specific gravity of 1.064 or above compared to the control mean of 1.046. Secondly an increased incidence of 1+ bilirubinuria has also been noted in historical controls and therefore this change was interpreted to be not treatment-related.

Two of twelve males gavaged with 250 mg/kg/day had blood (4+) in the urine. The reason for the hematuria in these two animals was not apparent as their individual prothrombin times (13.6 and 13.9 seconds, respectively) were within the range of the concurrent controls (11.6 - 14.5 seconds) and there were no gross or histological indications of hemorrhage, inflammation, or trauma in the urinary tract examined.

Anatomic pathology: There were no treatment-related differences in any of the organ weights for male or females at any dose level.

Gross pathology: Three animals died spontaneously during the course of the study. In each case the lesions were consistent with inadvertent gavage complications which was the cause of death.

Gross observations in the lungs such as, generalized edema, pale/dark focus, froth and mottled lungs were consistent with gavage complications observed at scheduled necropsy.

Histopathologic observations: There were no treatment-related histopathological changes attributed to the direct systemic toxicity of Dowfax 8390.

The lungs and trachea of some animals of both sexes gavaged with 25, 75 or 250 mg/kg/day had histopathologic changes consistent with aspiration into the respiratory tract following reflux of the test material (possibly due to the surfactant properties of the test material) that may have occurred during the course of repeated oral gavage and/or inadvertent gavage errors (Table 5). These changes consisted of very slight, slight or moderate, multifocal, chronic/chronic-active inflammation of the bronchi, bronchioles and the alveoli. Very slight to slight perivascular eosinophilic inflammation was seen in the lungs of some males and females, with or without inflammatory changes in the airways. The perivascular eosinophilic inflammatory response was interpreted to be a part of the inflammatory reaction triggered by the inadvertent entry of Dowfax 8390 into the respiratory tract during the process of repeated oral gavage. A very slight degree of perivascular eosinophilic inflammation was, however, seen in

one control female, the reason for which was not apparent. All these changes were random in distribution and did not involve all of the lung lobes.

Test substance : Disodium hexadecyldiphenyloxide disulfonate and disodium dihexadecyldiphenyloxide disulfonate constituted 36.7 ± 0.06% of the sample. The test material also contained small amounts of sodium sulfate (1.5% maximum) and sodium chloride (< 1%) with the balance comprised of water. Infrared spectroscopy was used to confirm the proposed structure of Dowfax 8390 surfactant.

Attached document :

Text Table 1. Prothrombin Time – Statistically Identified Differences

Parameter	Historical Control Data: Study 1[a]	0 MKD	25 MKD	75 MKD	250 MKD
Prothrombin Time(males)	12.1	12.4	13.2	**14.8***	**16.7***
Prothrombin Time (female)	11.8	12.0	12.0	11.7	11.3*

[a] Inhalation study conducted in 2003
* Statistically different from control mean (alpha = 0.05).
Bold type indicates treatment related effect.

Text Table 2. Clinical Chemistry – Statistically Identified Differences (Males)

Parameter	Historical Control Data: Study 1[a]	Study 2[a]	Study 3[b]	0 MKD	25 MKD	75 MKD	250 M
Urea Nitrogen (mg/dl)	15	13	14	17	16	14*	15
ALT (u/l)	29	33	32	47	40	40	**83**
Total Protein (g/dl)	6.4	6.3	6.2	6.6	6.5	6.4	6.3

[a] Inhalation studies
[b] Oral gavage study (The two inhalation studies and the one oral gavage study were done since 2000)
* Statistically different from control mean (alpha = 0.05)
Bold type indicates treatment-related effect.

Text Table 3. Clinical Chemistry – Statistically Identified Differences (Females)

Parameter	Historical Control Data: Study 1[a]	Study 2[a]	Study 3[b]	0 MKD	25 MKD	75 MKD	250 MKD
ALT (u/l)	36	63	27	30	31	33	**69***
AST (u/l)	94	120	107	77	76	78	**96***

[a] Inhalation studies
[b] Oral gavage study (The two inhalation studies and the one oral gavage study were done since 2000)
* Statistically different from control mean (alpha = 0.05)
Bold type indicates treatment-related effect.

Text Table 4. Urinalysis (Males)

Parameter	Historical Control Data		0 MKD	25 MKD	75 MKD	250 MKD
	Study 1[a]	Study 2[b]				
Volume (ml)	7.2	9.7	14.3	14.1	13.1	10.3
Specific Gravity	1.067	1.057	1.046	1.043	1.049	1.059
pH	7.0 (3) 7.5 (4) 8.0 (2) 8.5 (3)	7.0 (1) 7.5 (3) 8.0 (1) 8.5 (3) ≥ 9 (3)	7.0 (1) 7.5 (1) 8.0 (7) 8.5 (3)	8.0 (2) **8.5 (6)** **≥ 9 (3)**	**8.5 (10)** **≥ 9 (2)**	7.5 (1) 8.0 (1) 8.5 (1) **≥ 9 (9)**
Bilirubin	Neg (7) + (5)	Neg (9) + (2)	Neg (11) + (1)	Neg (10) + (1)	Neg (11) + (1)	Neg (7) + (5)
Blood	Neg (10) + (2)	Neg (10) + (1)	Neg (11) + (1)	Neg (11)	Neg (12)	Neg (10) ++++ (2)

[a] Inhalation study
[b] Oral gavage study (The inhalation and the oral gavage studies were done since 2000)
Bold type indicates treatment-related effect.

Text Table 5. Gavage Induced Lesions of the Lungs and Trachea

Sex	Males				Females			
Dose (MKD)	0	25	75	250	0	25	75	250
Number Examined	12	12	12	12	12	12	12	12
Lung Inflammation; chronic; bronchi-bronchiole; bronchiolo-alveolar; multifocal *Very slight*	0	0	0	0	0	0	0	1
Slight	0	0	1	0	0	0	0	1
Moderate	0	0	0	2	0	0	0	0
Inflammation; chronic active; bronchi-bronchiole; bronchiolo-alveolar; multifocal *Very slight*	0	0	0	1	0	0	0	0
Slight	0	0	1	0	0	0	0	1
Moderate	0	0	1	0	0	0	0	0
Inflammation; eosinophilic; perivascular; multifocal *Very slight*	0	2	1	1	1	1	0	1
Slight	0	0	1	1	0	0	1	1
Inflammation; chronic; pleura; focal *Slight*	0	0	0	1	0	0	0	0
Trachea Hyperplasia;regenerative, epithelium; diffuse *Very slight*	0	0	1	0	0	0	0	0
Slight	0	0	1	1	0	0	0	0
Inflammation; subacute to chronic; lamina propria; submucosa; focal *Slight*	0	0	0	0	0	0	0	1

Attached document : DOWFAX 8390 SURFACTANT: A COMBINED REPEATED DOSE TOXICITY STUDY WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN CD RATS

TABLE 24. Reproduction Indices and Pup Survival

DOSE MG/KG/DAY	0	25	75	250
NUMBER OF MALES	12	11*	12	12
NUMBER OF FEMALES	12	12	12	12
MALE MATING INDEX [A]	100 (12/12)	100 (11/11)	100 (12/12)	100 (12/12)
FEMALE MATING INDEX [B]	100 (12/12)	100 (11/11)	100 (12/12)	100 (12/12)
MALE CONCEPTION INDEX [C]	91.7 (11/12)	81.8 (9/11)	91.7 (11/12)	83.3 (10/12)
FEMALE CONCEPTION INDEX [D]	91.7 (11/12)	83.3 (10/12)	91.7 (11/12)	83.3 (10/12)
MALE FERTILITY INDEX [E]	91.7 (11/12)	81.8 (9/11)	91.7 (11/12)	83.3 (10/12)
FEMALE FERTILITY INDEX [F]	91.7 (11/12)	83.3 (10/12)	91.7 (11/12)**	83.3 (10/12)
GESTATION INDEX [G]	100.0 (11/11)	100.0 (10/10)	100.0 (10/10)	100.0 (10/10)
GESTATION SURVIVAL INDEX [H]	100 (166/166)	97.9 (139/142)	98.4 (127/129)	98.7 (149/151)
DAY 1 SURVIVAL INDEX [I]	100 (166/166)	100 (139/139)	96.9 (123/127)	98.7 (147/149)
DAY 4 SURVIVAL INDEX [I]	98.8 (164/166)	99.3 (138/139)	96.1 (122/127)	97.3 (145/149)

DOWFAX 8390 SURFACTANT: A COMBINED REPEATED DOSE TOXICITY STUDY WITH THE REPRODUCTION/DEVELOPMENTAL TOXICITY SCREENING TEST IN CD RATS

TABLE 24. Reproduction Indices and Pup Survival (continued)

DOSE MG/KG/DAY	0	25	75	250
POSTIMPLANTATION LOSS %[J]	5.69 ± 6.00	9.07 ± 10.55	12.61 ± 13.13	7.48 ± 10.647
SEX RATIO ON DAY 1				
MALE:FEMALE	47:53	49:41	53:47	51:49
GESTATION LENGTH				
(DAYS)	21.6 ± 0.5	21.6 ± 0.5	21.8 ± 0.6	21.6 ± 0.5
TIME TO MATING				
(DAYS)	2.7 ± 1.7	2.1 ± 1.1	1.8 ± 1.1	2.2 ± 1.2

* MALE 5569 DIED EARLY AFTER TWO DAYS OF COHOUSING WITH FEMALE 5617 FOR BREEDING. FEMALE WAS GIVEN TO NEXT AVAILABLE MALE AND MALE 5569 WAS EXCLUDED FROM CALCULATIONS OF MALE REPRODUCTIVE INDICES.
** FEMALE 5692 DIED DURING GESTATION, BUT WAS FOUND TO BE PREGNANT WITH NORMALLY DEVELOPED FETUSES AND WAS THEREFORE INCLUDED IN THE CALCULATION OF FEMALE FERTILITY.
[A] # MALES WHICH MATED RESULTING IN A SPERM + VAGINAL LAVAGE OR PREGNANT/TOTAL # MALES AND FEMALES COHOUSED X 100%.
[B] # FEMALES WHICH WITH A SPERM + VAGINAL LAVAGE OR PREGNANT WITHOUT ADITIONAL EVIDENCE OF MATING/#FEMALES COHOUSED WITH MALES X 100%.
[C] # MALES SIRED A LITTER/# MALES MATED X 100%.
[D] # FEMALES DELIVERING A LITTER/# FEMALES MATED X 100%.
[E] # MALES WHICH SIRED A LITTER/# MALES AND # FEMALES COHOUSED X 100%.
[F] # FEMALES DELIVERING A LITTER/# FEMALES COHOUSED WITH MALES X 100%.
[G] # FEMALES DELIVERING A LIVE LITTER/# FEMALES DELIVERING A LITTER X 100%.
[H] PERCENTAGE OF NEWBORN PUPS THAT WERE ALIVE AT BIRTH
[I] # OF LIVE PUPS ON DAY 1 OR 4 /# OF LIVE PUPS ON DAY 0 X 100%.
[J] MEAN PERCENT/LITTER (CALCULATED AS [NO. IMPLANTS - NO. VIABLE OFFSPRING]/NO IMPLANTS) X 100
THERE WERE NO STATISTICALLY IDENTIFIED DIFFERENCES FROM THE CONTROL MEAN AT ALPHA = 0.05.

Conclusion : The No-Observable-Adverse-Effect Level (NOAEL) for general toxicity was 25 mg/kg/day, while 250 mg/kg/day was a no-observable-effect level (NOEL) for reproductive and neurological effects. Gavage administration of 250 mg/kg/day of Dowfax 8390 resulted in increased incidences of soft/decreased feces (males only), accompanied by slightly increased prothrombin times (males only), increased serum ALT (both sexes) and increased serum AST (females only) levels. At 75 mg/kg/day, prothrombin times were increased in males only. No toxicologically significant effects occurred in the 25 mg/kg/day group. Various respiratory symptoms were considered the result of gavage related aspirations of the surfactant test material. Urinalysis (conducted in males only) revealed a slight increase in urine pH at all dose levels thought to be associated with the properties of the test material and/or its metabolites, but with no toxicological sequelae.

Reliability : (1) valid without restriction
1a: GLP guideline study

24.05.2006 (48)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1) Cardinaals, J.M., Determination of the Melting Point/Melting Range of Dowfax 8390, RCC NOTOX Study Ref. No. 0910/C598, July 1988 for Dow Chemical Rheinwerk, Rheinmunster, Germany, unpublished report created for Dow.

(2) The Dow Chemical Company, 2001.

(3) Cardinaals, J.M., Determination of the Boiling Point/Boiling Range of Dowfax 8390, RCC NOTOX Study Ref. No. 0910/C599, July 1988, for Dow Chemical Rheinwerk, Rheinmunster, Germany, unpublished report created for Dow.

(4) Cardinaals, J.M., Determination of the Density of Dowfax 8390, RCC NOTOX Study Ref. No. 0910/C600, July, 1988, for Dow Chemical Rheinwerk, Rheinmunster, Germany, unpublished report created for Dow.

(5) Corbett, P., Schmitz, A., Determination of the Surface Tension of Aqueous Solution of Dowfax 8390, Separation System & Process Products Report 222/88, October, 1988, Dow Chemical Europe, Rheinmuenster, Germany, unpublished Dow report.

(6) Gladdines, M.M., NOTOX, The Netherlands, Dowfax* 8390-D Anionic Surfactant: Determination of the Hydrolysis as a Function of pH, DET 2295, 21 July, 1995, unpublished Dow report.

(7) Gladdines, Ir. M. M., TNO (Delft), The Netherlands, Dowfax* 8390-D Surfactant: Soil Adsorption/Desorption Screening Test (OECD 106), DET 2297, 25 July 1995, unpublished Dow report.

(8) Coenen, Ir.T.M.M., Ready Biodegradability: Closed Bottle Test with Dowfax* 8390, DET 1330, 25 January, 1990, XD-8390-023, unpublished report created for Dow.

(9) Gonsior, S.J., Goodwin, P.A., Biodegradation of a Linear Monoalkylated (C16 Chain Length) Di-Sulfonated Diphenyl Oxide Surfactant (MADS) in Aquatic Sediments, HET T3.02-000-000-304, 22 November, 1999, 981136, unpublished Dow report.

(10) Rhinehart, W.L., and Bailey, R.E., Biodegradability of Dowfax XD 8390 by the Soap & Detergent Association Confirming Test (Semi-Continuous Activated Sludge), Report ES-128, July 11, 1977, unpublished Dow report.

(11) Gonsior, S.J., Markham, D.A., The Biodegradation of a Linear Monoalkylated (C16 Chain Length) Di-Sulfonated Diphenyl Oxide Surfactant (MADS), ES-2811, July 10, 1996, T3.02-000-000-006, unpublished Dow report.

(12) Schleheck, D., Cook, A., University of Konstanz, Germany, Dowfax* 8390: Side-Chain Oxidation and Desulfonation, DET 2656, 20 November, 1998, DR-0140-7814-008, unpublished report created for Dow.

(13) Gonsior, S.J., Generation of Activated Sludge Effluent Containing Dowfax* 8390 Surfactant Biodegradation Products, ES-3082, September 17, 1996, unpublished Dow report.

(14) Gonsior, S.J., Radtke, B.J., Stock, M.K., Generation of Activated Sludge Effluent Containing Dowfax 8390 Surfactant Biodegradation Products, HET XD-008390-032, 19 December, 2000, 001187, unpublished Dow report.

(15) Rhinehart, W.L., Biodegradability of Dowfax XD 8390 (lots 09254 and 10154), 1:128 and 1:256 Desinfectant [sic] Formulations by the Soap and Detergent Association Confirming Test. (Semicontinuous Activated Sludge), ES-8, Nov. 26, 1974, unpublished Dow report.

(16) Gonsior, S.J., Semi-Continuous Acitvated Sludge Biodegradability Test for Experimental Surfactants XDS 8174.00, XDS 8292.00, and Dowfax 2A1, ES-932, January 8, 1987, T3.02-000-000-008, unpublished Dow report.

(17) Cardinaals, J.M., Determination of the Fat Solubility of Dowfax 8390, RCC NOTOX Study Ref. No. 0910/C601, August 5, 1988, for Dow Chemical Rheinwerk, Rheinmuenster, Germany, unpublished report created for Dow.

(18) Miller, J.A., Brown R.P., Landre, A.M., Evaluation of the Acute Toxicity from the Generation of Activated Sludge Effluent Containing Representative Aquatic Organisms, ES-3097, May 14, 1996, unpublished Dow report.

(19) Alexander, H.C., Rhinehart, W.L., Static Acute Fish Toxicity of Dowfax* XD-8390 to Fathead Minnows, March 17, 1975, XD-8390-010. (unpublished Dow letter report)

(20) Bogers, M., Welboren, G.T.C., Dowfax* XD 8390: Acute Toxicity Study with Rainbow Trout, DET 981, November 25, 1987, XD-008390-017, unpublished report created for Dow.

(21) Bogers, M., Welboren, G.T.C., NOTOX, The Netherlands, Dowfax* XD 8390: Assessment of the Acute Effects on the MObility of Daphnia magna, DET 982, 25 Nov., 1987, XD-008390-018, unpublished report created for Dow.

(22) Bogers, NOTOX, The Netherlands, Dowfax 8390-D: Acute Toxicity to Selenastrum capricornutum (OECD Algae Growth Inhibition Test), DET 2293, 11 July, 1995, unpublished report created for Dow.

(23) Koopmans, M.J.E., NOTOX, The Netherlands, Dowfax 8390-D Surfactant: Activated Sludge Respiration Inhibition Test, DET 2271, May 22, 1995, unpublished report created for Dow.

(24) Henry, K.S., Dowfax 8390 Surfactant Degradation Products: 21-Day Chronic Toxicity Study with the Daphnid, Daphnia magna Straus, unpublished Dow report, 27 February, 2001, 001162.

(25) Bogers, M., NOTOX, The Netherlands, Dowfax 8390-D: Daphnia Magna Reproduction Test, DET 2389, 5 March, 1996, unpublished report created for Dow.

(26) Coles, R.J., Safepharm Laboratories, UK, Dowfax* 8390 Surfactant: Acute Oral Toxicity (Limit Test) in the Rat, DET 1620, 15 March, 1991, XD-8390-025, unpublished report created for Dow.

(27) Zucker, A.M.M., Reijnders, J.B.J., Dowfax XD 8390: Evaluation of Acute Oral Toxicity in the Rat, DET 977, November 25, 1987, XD-8390-013, unpublished report created for Dow.

(28) Gilbert, K.S., Dowfax 8390: Acute Toxicological Properties, HET DR-008390-009, 16 March, 1995, unpublished Dow report.

(29) Wall, J.M., XU-40341.00 Dowfax* 8390, Powder Form: Acute Toxicologic Properties, HET XD-008390-006, August 3, 1987, unpublished Dow report.

(30) Henck, J.W., Acute Toxicological Properties and Industrial Handling Hazards of XD 8390, HET-XD-8390-(5), February 19, 1980, unpublished Dow report.

(31) Rampy, L.W., Keeler, P.A., Yakel, H.O., Toxicological Properties and Industrial Handling Hazards of XD-8390, HET XD-8390-(1), August 12, 1974, unpublished Dow report.

(32) Coles, R.J., SafePharm Laboratories, UK, Dowfax* 8390 Surfactant: Acute Dermal Toxicity (Limit Test) in the Rat, DET 1686, 23 April, 1991, XD-8390-029, unpublished report created for Dow.

(33) Reijnders, J.B.J., Zucker-Keizer, A.M.M., NOTOX, The Netherlands, Dowfax* XD 8390: Evaluation of Acute Dermal Toxicity in the Rat, DET 978, November 25, 1987, XD-8390-014, unpublished report created for Dow.

(34) Brooks, K.J., Dowfax* 8390: Primary Dermal Irritation Study in New Zealand White Rabbits, unpublished Dow report, 11 August, 1997, 971134.

(35) Coles, R.J., SafePharm Laboratories, UK, Dowfax* 8390 Surfactant: Acute Dermal Irritation Test in the Rabbit, DET 1621, 15 March, 1991, XD-8390-026, unpublished report created for Dow.

(36) Weterings, P.J.J.M., Daamen, P.A.M., NOTOX, The Netherlands, Dowfax* XD 8390: Assessment of Primary Skin Irritation/Corrosion Potential in the Rabbit, DET 980, November 25, 1987, XD-8390-016, unpublished report created for Dow.

(37) Brooks, K.J., Dowfax* 8390 Surfactant (5% Aqueous Solution): Acute Primary Eye Irritation Study in New Zealand White Rabbits, unpublished Dow report, 2 February, 1998, 971196.

(38) Coles, R.J., SafePharm Laboratories, UK, Dowfax* 8390 Surfactant: Acute Eye Irritation Test in the Rabbit, DET 1622, 15 March, 1991, XD-8390-027, unpublished report created for Dow.

(39) Weterings, P.J.J.M., Daamen, P.A.M., NOTOX, The Netherlands, Dowfax* XD 8390: Assessment of Acute Eye Irritation/Corrosion Potential in the Rabbit, DET 979, November 25, 1987, XD-8390-015, unpublished report created for Dow.

(40) Busschers, M., NOTOX B.V., The Netherlands, Assessment of Contact Hypersensitivity to Dowfax* 8390-D in the Albino Guinea Pig (Maximisation Test), DET 2637, 20 August, 1998, unpublished report created for Dow.

(41) Coles, R.J., SafePharm Laboratories Ltd., Dowfax* 8390 Surfactant Solution: Magnusson & Kligman Maximisation Study in the Guines Pig, DET 1545, 2 February, 1991, XD-8390-024, unpublished report created for Dow.

(42) Coles, R.J., SafePharm Laboratories, UK, Dowfax* 8390 Surfactant: Buehler Delayed Contact Hypersensitivity Study in the Guinea Pig, DET 1623, 15 March, 1991, XD-8390-028, unpublished report created for Dow.

(43) Berdasco, N.M., Dowfax* 8390: Dermal Sensitization Potential in the Hartley Albino Guinea Pig, HET XD-008390-007, March 21, 1991, unpublished Dow report.

(44) Berdasco, N.M., 2.9% Dowfax* 8390: Dermal Sensitization Potential in the Hartley Albino Guinea Pig, HET XD-008390-008, March 26, 1991, unpublished Dow report.

(45) Weterings, P.J.J.M., Debets, F.M.H., NOTOX, The Netherlands, Dowfax XD 8390: Assessment of Skin Sensitization Potential in the Guinea Pig, DET 976, November 25, 1987, XD-008390-012, unpublished report created for Dow.

(46) Schwetz, B.A., Humiston, C.G., Kociba, R.J., Dowfax* Surfactant XD-8390: Results of a 90Day Dietary Feeding Study in Rats, HET XD-8390-(3), February 11, 1976, unpublished Dow report.

(47) Cummins, H.A., Ashby, R., Fowler, J.S.L., Life Sciences Research, Dowfax* XD 8390: Four Week Toxicity Study by Oral Administration to CD Rats, DET 985, November 26, 1987, XD-008390-022, unpublished report created for Dow.

(48) Carney, E.W., Liberacki, A.B., Maurissen, J.P. and Thomas, J. (2003). Dowfax 8390 surfactant: A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in CD rats. Unpublished report of The Dow Chemical Company.

(49) Schwetz, B.A., Humiston, C.G., Wade, C.E., Kociba, R.J., Kalnins, R.V., LeBeau, J.E., Dowfax* Surfactant XD-8390: Results of a 90-Day Dietary Feeding Study in Dogs, HET XD-8390-(4), February 10, 1976, unpublished Dow report.

(50) Enninga, I.C., NOTOX, The Netherlands, Dowfax* XD 8390: Evaluation of the Mutagenic Activity in the Ames Salmonella Reverse Mutation Assay, DET 984, November 26, 1987, XD-008390-021, unpublished report created for Dow.

(51) Enninga, I.C., NOTOX, The Netherlands, Dowfax* XD 8390: Chromosomal Aberration Assay with Cultured Peripheral Human Lymphocytes in vitro, DET 983, November 26, 1987, XD-008390-020, unpublished report created for Dow.

(52) Linscombe, V.A., Day, S.J., Evaluation of Dowfax* 8390D Surfactant in an In Vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes, unpublished Dow report, 12 June, 1998, 971201.

(53) Linscombe, V.A., Shisler, M.R., Evaluation of Dowfax* 8390-D Surfactant in the Chinese Hamster Ovary Cell/Hypoxanthine-Guanine-Phosphoribosyl Transferase (CHO/HGPRT) Forward Mutation Assay, unpublished Dow report, 5 February, 2001, 001106.

(54) Johnston, R.V., Schwetz, B.A., Mensik, D.C., Lisowe, R.W., Cytogenetic Effects of Dowfax* Surfactnat XD-8390 on Rat Bone Marrow Cells, HOM-77-3, July 20, 1977, unpublished Dow report.

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT